BUREAU OF HYGIENE AND TROPICAL DISEASES.

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BERIBERI.

DE LANGEN (C. D.). **The International Control of Beri-Beri.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 61–85.

The author states that partly decorticated rice is not a satisfactory article for international trade. Polished rice, therefore, which keeps better, is used for food. Rice in the husk, however, can be kept for years and is suitable for transport and storage, but owing to its greater bulk must be more expensive. He recommends it for use in the Dutch Indies. He thinks better use should be made of the bran, which is now given to cattle and pigs; the finest polishings could be used with wheaten flour, but the product is not very palatable and is not likely to be of much practical value.

Very little or nothing can be done internationally in the control of beriberi; local conditions and possibilities are the most important factors.

P. W. Bassett-Smith.

CHUN (J. W. H.) & WU LIEN TEH. **Beri-Beri Control from an Administrative Standpoint.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Toyko, 1925.* Vol. 1. pp. 153–165. [37 refs.]

The author emphasizes the importance of combined legislative and educative measures, and of subsidizing rice mills which will produce proper rice. Taxation of white rice is impracticable. The importance of good hygiene should be taught in addition to careful dieting, as well as the early recognition and treatment of cases.

P. W. B–S.

KATSURADA (F.), IZUMI (M.) & KUBO (K.). **Some Reports of the Institute for Seamen's and Tropical Diseases, Kobe.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 819–820.

The authors report that during the past ten years out of 7,552 cases in the Mercantile Marine there were 710 of beriberi, or 9·4 per cent. Since a diet of 70 per cent. rice and 30 per cent. of barley has been enforced with other hygienic measures, there has been a considerable reduction of cases, yet many are still reported. It is noted that pernicious malaria favours the onset of severe beriberi.

P. W. B–S.

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Shimazono (J.). **On the Etiology of Beri-Beri.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 37–60.

The author states that there are many changes common to beriberi and avitaminosis. The chief differences are that in beriberi there is cardiac hypertrophy with tachycardia, anorexia, oedema, rise of blood sugar and reduced gastric secretion, whereas in avitaminosis there is no cardiac hypertrophy, but marked emaciation, atrophy of viscera, and hypertrophy of the cortex of the suprarenals.

P. W. B–S.

Omori (Kenta). **Studies on the Cause and Treatment of Beri-Beri in Japan.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 183–204.

The author particularly draws attention to the high death rate in soldiers and sailors and in infants. The causes are indirect and direct (vitamin B deficiency). Preventive measures are urgently required, as there were 10,000 deaths in 500,000 cases, generally in young people at the most productive period of life. Italian millets and corn are recommended. Improvement in general hygiene is urgent.

P. W. B–S.

Sugimoto (K.), Yasuda (Y.), Higuchi (M.), Momoyeda (S.) & Tanaka (S.). **Studies on Digestibility and Utilization of Rice in Different Methods of Cooking.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 263–268.

Sugimoto (K.). **Studies on the Digestibility and Utilization of Rice of Different Grades of Polishing.**—*Ibid.* pp. 269–271.

The various methods of cooking and the different products turned out are described, but are only of local interest. The degree of digestibility depended upon the grade of rice, the caloric value of polished rice being higher than that of unpolished. The percentage of nitrogen in the urine was increased when the subjects consumed polished rice, though the urea nitrogen was less. With unpolished rice the phosphorus in the urine was increased and the total quantity of the faeces was larger. Therefore to obtain a food of similar value more unpolished than polished rice must be consumed.

P. W. B–S.

Deggeller (O.). **On the Means of testing Rice with a View on its causing Beriberi.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 87–90. With 9 figs. on 2 plates.

Various methods have been described of determining the characters of rice and their vitamin value. The author stained the grains with an iodine solution which gave varying amounts of blueness in accordance with the extent of decortication and tried to get coloured photograph plates for general use, but these were not permanent. He therefore had coloured prints made which can be used for " controls " and are largely in demand.

P. W. B–S.

TANAKA (Shizuo) & ENDO (Masaharu). Ueber den Stoffumsatz bei Kakke und Geflügerberiberi. [**On the Metabolism in Kakke and Bird Beriberi.**]—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 148–151.

The authors summarize the results of their experiments, which show that in kakke and bird beriberi there is a notably increased production of lactic acid and that in bird beriberi the oxygen taken up and CO_2 given off is distinctly lower than the normal. It is impossible to say whether this is due to a reduced oxygen supply or to lessened chemical activity of the oxidizable substance. Through the abnormal metabolism in bird beriberi different intermediate products are produced, as is shown by the low respiratory quotient and increase of lactic acid. They consider that the abnormal metabolic changes in kakke and bird beriberi are identical.

P. W. B–S.

FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE. **Report of the Sixth Congress of the Far Eastern Association of Tropical Medicine.** 1925. Oct. 11–31. 114 pp. Tokyo, Japan.

This booklet contains the opening and closing addresses, reports of council meetings, and the resolutions passed by the Congress. Of general interest are the statements laid before the Committee on Beriberi Control.

Dr. R. TAKANO, representative of the Japanese Government, pointed out that it is exceedingly difficult in Japan to prohibit the use of polished rice as food or by administrative measures restrict the degree of its refinement. Rice is a more important food for the Japanese than bread for the European, and has been the staple food for ages. Not only is the refining process now carried further than formerly, but the practice of adding other cereals to rice is disappearing. Nevertheless no large number of persons has contracted beriberi. He would rely on educational methods. In any case, the methods of cooking are such that the water-soluble ingredients are largely diminished by washing, and unpolished rice treated in the same way would suffer the same loss. To make any abrupt change in the method of cooking would be difficult. As to the effects of transport and storage, rice in Japan is stored as unpolished rice, but this does not make for the prevention of beriberi, for the customers polish and wash it before it reaches the table. Unpolished foreign rice appears to be unfit for long storage on account of fermentation and damage from insects. He notes that half-polished rice is not so well absorbed in the intestine as refined rice, 94·4 as against 97 per cent.

Dr. LUHN, Chief Health Officer, Sarawak, gave the results of a questionary, but does not state who furnished the replies. He notes that beriberi in Sarawak is mainly found in places where imported Chinese labour is used and is rare among Javanese imported labour as well as in Malays. " Before proceeding to the more severe restrictions it seems desirable to legislate for the better feeding of imported labour, especially Chinese," making vegetable gardens compulsory as well as the addition of oil and a minimum of meat or fish to the ration.

A summary is given of Colonel MCCARRISON's Memoir on the Relation of rice to beriberi in India [see this *Bulletin*, Vol. 22, p. 594]. Though rice-eating races are widely distributed throughout India, beriberi as an endemic in confined to certain well-defined and narrow areas,

especially in Madras, and has been so confined for the last hundred years. Strict rice-eating Hindus in these areas suffer less from beriberi than classes of the community who do not restrict themselves to rice. Millet eaters here suffer from beriberi: millet eaters outside do not. Beriberi originates only in those jails which are in the endemic area, though the diet scale in all Madras jails is the same. Madrassi troops furnished 90 per cent. of cases of beriberi in the Native army between the years 1900 and 1920, though they formed no more than one-sixth of its total strength. He notes parboiling is an efficient means of "fixing" vitamin B in the rice grain "for subsequent milling, even when high polishing is resorted to, does not deprive the rice grain of more than one-third of its original content of this vitamin." Chemical investigations in India (NORRIS) have failed to substantiate the claim that the phosphorus pentoxide content of rice can always be regarded as a reliable index of "the beriberi preventing" properties of rice. He believes that there are two factors concerned in the causation of beriberi (*a*) a nutritional or intrinsic; (*b*) an unknown, extrinsic, this unknown factor being peculiar to certain tracts of country or certain places or individuals and to be found either in the gastrointestinal tract of sufferers or in deteriorated food. The control of the disease in India is a matter of education for improvement in the standard of living of the people, housing, sanitation, diet, and storage of rice and other food.

Dr. VERVOORT, speaking for Sumatra, reported that only on the East Coast of Sumatra was imported rice used, and chiefly for the use of large plantations; legal action in rice control is unnecessary.

The Committee on Beriberi Control passed the following resolutions, which were accepted by the Council.

I.

"Whereas beriberi is known to prevail extensively in many countries of the Far East; and

"Whereas there is enormous loss of life, with corresponding invalidism and disability, due to deficient diet; and

"Whereas the deficiency may be corrected by the use of freshly under-milled rice or by the addition of accessory foods; and

"Whereas notwithstanding extensive research work in many countries nothing has been put forward to controvert the disappearance of beriberi when an adequate diet is used; and

"Whereas a suitable test is desirable to determine the presence of sufficient vitamin B and accessory substances in rice; and

"Whereas educational measures to promote the use of adequate diets are highly desirable:

"Therefore be it resolved that this Sixth Congress of the Far Eastern Association of Tropical Medicine considers it urgently desirable that where over-milled rice forms a staple diet steps should be taken to discourage the use of rice from which essential food factors have been removed and that safe storage be provided for under-milled rice and furthermore that the use of accessory foods be encouraged: and

"Therefore be it further resolved that the F.E.A.T.M. considers beriberi a preventable disease and that each country be urged to take vigorous measures to combat its ravages; and

"Therefore be it further resolved that all countries of the East make beriberi a notifiable disease and that arrangements be made for publication of statistics by the Eastern Bureau at Singapore; and

"Therefore be it further resolved that governments encourage research toward developing a practical test for rice that may cause beriberi when used as a staple article of diet.

II.

"Whereas there is no definite understanding as to the classification of rice in its different stages during the process of milling; and

"Whereas it is believed necessary that studies on beriberi be continued in the different Far Eastern countries:

"Therefore be it resolved to recommend that the Beriberi Committee be continued, and that facts be collected which might be used in classifying rice in its different stages in the process of milling."

A. G. B.

Kato (Toyojiro). [**A Report on the Epidemic of Beriberi Occurring in a School Dormitory. Together with a Notice on the Vitamin Contents of Barley.**]—*Tokyo Iji-Shinshi* (*Tokyo Med. News.*). 1926. June. No. 2474. [Summarized in *Japan Med. World.* 1926. Oct. 15. Vol. 6. No. 10. p. 286.]

The author reports on a small epidemic of beriberi in one dormitory of a school in Sendai. The students in this room were all new comers and received a rice to barley ration with the proportion of 6-4, whereas the others had one of 7-3. Those served with the higher barley content contracted the disease more often than those served with the lesser. Experiments with pigeons showed that birds fed on the barley alone soon contracted so-called vitamin deficiency symptoms.

P. W. B–S.

Coyne (A. E.). **Beriberi: its Symptoms and Treatment.**—*Indian Med. Gaz.* 1927. Jan. Vol. 62. No. 1. pp. 17–19.

There is nothing new with regard to symptoms. The usual food precautions were taken. It is stated, though not demonstrated, that chilli in curry kills the vitamins in the vegetables. The author used marmite both as a prophylactic and for the cure of the disease. Rice-bran tea is easy to supply and is recommended.

P. W. B–S.

Mazzolani. Une épidémie de béribéri au Yunnan (Chine). [**An Epidemic of Beriberi in Yunnan.**]—*Rev. Méd. et Hyg. Trop.* 1927. Jan.–Feb. Vol. 19. No. 1. pp. 9–15. [6 refs.]

In Southern Yunnan the country is mountainous and large quantities of rice have to be brought in for the imported Chinese. In 1906–7 beriberi was very prevalent and there was a high mortality—30 to 47 per cent. The cause was traced to deteriorated and fermented rice and the disease was stopped by the substitution of red rice.

P. W. B–S.

Trabaud. Difficultés du diagnostic différentiel entre le béribéri humide et la bacillose péritonéale à forme ascitique chez les Sénégalais. [**Diagnosis between Wet Beriberi and Ascitic Bacillary Peritonitis in Senegalese.**]—*Rev. Méd. et Hyg. Trop.* 1926. Nov.–Dec. Vol. 18. No. 6. pp. 169–170.

At the hospital St. Jean, Beyrouth, there were among the Senegalese a number of cases of albuminuria with oedema, at first diagnosed as renal. The cause was, however, difficult to determine, since most had pulmonary signs and ascites. The diagnosis rested between peritonitis of bacillary origin and a form of wet beriberi. No evidence of tubercle could be obtained. The ascitic fluid showed numerous red blood cells

and flakes of endothelial cells, without lymphocytes or polynuclear cells. Though albumen was present in the urine there were no casts or other evidence of nephritis, so this was ruled out and a diagnosis of beriberi made by a process of exclusion.

P. W. B–S.

Bernard (P. Noël), Pons, (R.) & Lalung-Bonnaire. Les oedèmes dans le béribéri. [**Oedema in Beriberi.**]—*Bull. Soc. Path. Exot.* 1927. Jan. 12. Vol. 20. No. 1. pp. 30–33.

There is much that is of a text-book character in this paper. The chief points emphasized are the toxicity of the poison acting on the nerve cells and the action of fluid in different parts of the body which dilutes down the poison, " a reaction of defence." This is influenced by secondary factors such as intercurrent infections, generally alimentary, or defective hygienic conditions. The retention of chlorides and toxin may explain the pre-paralytic oedemas.

P. W. B–S.

Bernard (P. Noël), Bablet (J.) & Guillerm (J.). Le rein et les fonctions rénales dans le béribéri. [**The Kidney and its Functions in Beriberi.**]—*Bull. Soc. Path. Exot.* 1927. Jan. 12. Vol. 20. No. 1. pp. 39–44. With 4 figs. on 2 plates. [1 ref.]

It has been shown that in human beriberi there are changes in the urinary output and also lesions in the renal tubules. There is generally with the oedema a decided increase of chlorides in the blood. The authors argue that the absence of any true inflammatory nephritis strengthens the hypothesis that the disease is due to an infective germ or rather the toxic action of a germ. They state that the renal condition is exactly similar to that caused by the toxin of *B. asthenogenes* in young pigs suffering from the beriberi-like condition.

P. W. B–S.

Bernard (P. Noël) & Bablet (J.). Le coeur dans le béribéri. [**The Heart in Beriberi.**]—*Bull. Soc. Path. Exot.* 1927. Feb. 9. Vol. 20. No. 2. pp. 127–131.

The authors note that the heart of acute beriberi cases rarely shows any valvular lesions. The enlargement is due to myocardial changes with dilatation of the capillary vessels and lymphatics causing oedema, changes similar to those found in the experimental beriberi of piglets caused by infection with the *B. asthenogenes*. The heart lesions, therefore, of human beriberi have their origin in infectious toxins.

P. W. B–S.

Bablet (J.), Guérin (F.), Lalung–Bonnaire & Pons (R.). Examen radioscopique du coeur dans le béribéri. [**Radioscopy of the Heart in Beriberi.**]—*Bull. Soc. Path. Exot.* 1927. Feb. 9. Vol. 20. No. 2. pp. 131–132. With 1 plate.

Radiography shows that the cardiac shadow is at once increased in width and diminished in height, and these changes are exaggerated in the paralytic stage of the disease, when in consequence of failure of the muscles of respiration the diaphragm rises.

P. W. B–S.

Pons (R.) & Lalung-Bonnaire. Circulation et respiration dans le béribéri. [**The Circulation and Respiration in Beriberi.**]—*Bull. Soc. Path. Exot.* 1927. Feb. 9. Vol. 20. No. 2. pp. 132–138. With 3 text figs.

This is a study of the circulatory and respiratory systems in cases of beriberi observed in the Pasteur Institute at Saigon. The authors note that tachycardia is always synchronous with the onset of oedema and always precedes the nervous symptoms. In the later stages the tachycardia is increased and is more irregular and is due to cardiac irritability. In the oedematous stage there is increased blood pressure but in the atrophic paralytic stage the tension falls rapidly from the toxin acting upon the nervous system. This alteration of the blood pressure is of great prognostic value. In the heart of beriberics the two chief manifestations are instability and irritability, depending upon vagus and sympathetic involvement.

With regard to the respiratory system the early signs are oedema of the bases ; later the intercostals and diaphragm are paralysed, respiration is short, shallow and irregular, with some implication of the accessory muscles. Rarely there is at the time of cardiac crisis an acute pulmonary oedema.

P. W. B–S.

Heinemann (H.). Symmetrische Hauterscheinungen bei einem Beri-Beri-Kranken. [**Symmetrical Skin Symptoms in a Beriberi Patient.**]—*Dermat. Ztschr.* 1927. Apr. Vol. 50. No. 2. pp. 135–136. With 1 fig.

The author reports the case of a Chinaman treated in hospital, who had symptoms of beriberi, with paresis of muscles, dilated heart, and oedema, and also an exanthem especially marked upon the front of the hands and wrist, dorsum of feet and lower part of the legs. This was light brownish in colour, rough, scaly, with rounded margins. It was cured when the man was put upon anti-beriberi treatment. The author was not able from his incomplete observations to determine whether this pellagra-like condition was really dependent upon the beriberi, but he reports the case to stimulate further observations. There is a good photograph of the appearance of the feet and legs.

P. W. B–S.

Morin (H. G. S.), Advier (M.) & Marinot (J.). Note préliminaire sur les polynévrites observées à l'hôpital indigène de Cholon en janvier-août 1926. [**Cases of Polyneuritis seen at the Native Hospital, Cholon.**]—*Bull. Soc. Path. Exot.* 1927. Jan. 12. Vol. 20. No. 1. pp. 33–38. [1 ref.]

The authors state that there were in eight months at the hospital in Cholon, Cochin-China, 349 cases of beriberi out of a total of 5,296 admissions, that is 6·6 per cent. ; 95 per cent. of these are of the dry form. The diagnosis of true beriberi from other forms of peripheral neuritis is often difficult, and there is much slackness in making returns ; more care is required in the differentiation of organic nerve disease. The spinal changes as described by H. Wright & Glogner are accepted as present and the nerve endings in the muscles are thought to be the physiological elements on which the toxin acts, but of this no proof is brought forward.

P. W. B–S.

Vitug (Wenceslao). **Some Clinical Aspects of Acute Cardiac Beriberi in Adults.**—*Jl. Philippine Islands Med. Assoc.* 1926. Nov. Vol. 6. No. 11. pp. 380–392. With 7 charts. [1 ref.]

The author states that acute beriberi is characterized by a preponderance of cardiac symptoms, and is frequently accompanied by fever which may be intermittent, irregular, remittent or continuous. He gives a number of rules for differentiating the disease from other valvular lesions, all of which can be obtained from ordinary text books.

P. W. B–S.

Tsuzuki (Jinnosuke). **Clinical Experiences in the Antiberiberin Treatment against Beriberi.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 223–225.

Antiberiberin may be given as injections, powders or pills, and has been used since 1911. Over 12,000 cases have been treated since 1913. The symptoms improve in about a week, the disease is shortened, and the mortality reduced. The sequelae may not clear up for six months. In the beriberi of sucklings it has been most successful, 334 cases treated in six years, and all cured. The dose for the babe is the same as that for an adult and the duration of treatment is about 5 days.

P. W. B–S.

Suzuki (U.).) **Chemical Studies of Vitamin-B in Japan.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 27–35. [24 refs.]

The author describes how he first prepared and used "oryzanin," It has the chemical composition of other vitamin B. preparations, most of which contain sulphur. These amino-acid compounds can be purified, but much further work is required to determine fully their physiological characters.

P. W. B–S.

Fujimaki (Y.) & Matsumuro (H.). **The Vitamin B Content of Rice. New and Old Rice, also Different Grades of Polishing.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 233–237.

The authors found that unpolished rice which had been stored for one year lost about 40 per cent. of its vitamin B. Their experiments were made with pigeons and white rats. Taking the antineuritic vitamin of unpolished rice as 100, then that of 50 per cent. polished was 55 and of 70 per cent. 43. That of white well-polished rice was 25, and of white rice polished with sand paper nil. The vitamin B content diminishes with the period of preservation and with the different grades of polishing, and these run parallel, according to Higuchi, with the diminished catalytic action of the enzyme oxidase.

P. W. B–S.

Higuchi (Taro). **The Chemical Changes of Rice during Preservation.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 259–262.

The author found that the curve representing the decrease of vitamin B was approximately parallel to the curve of the decrease

in catalytic activity. This is of practical utility in determining the value of the rice (see FUJIMAKI and MATSUMURO). The oxidase reaction is used to distinguish old rice from new ; the latter becomes purple in colour, the former is not coloured.

P. W. B–S.

HIGUCHI (T.), KONDO (M.), HARA (M.), NARITA (S.) & MATSUZAWA (K.). **Relationships between the Chemical Composition of Rice and the Different Grades of Polishing.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1 pp. 253–258.

This is a paper full of tables of figures to which interested persons must refer. The authors state that there are many good reasons, from both physiological and economic stand-points, for recommending 70 per cent. polished rice. It contains about 0·5–0·8 per cent. of phosphorus (polished rice has 0·4). This view was questioned by HEISER, who stated that age and condition of storage must be taken into account.

P. W. B–S.

TAKAHIRA (Hideo) & KITAGAWA (Sadayoshi). **Respiratory Metabolism after the Ingestion of Rice of Different Grades of Polishing.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 273–277.

This paper follows those on the digestibility and utilization of rice, and in it the authors demonstrate the changes in the respiratory metabolism caused by the use of different grades. They found that the ingestion of rice raised the metabolism and respiratory quotient above the normal, especially when polished rice was used. " The difference of the utilized calories was too small to influence the different specific dynamic actions on metabolism." They conclude that polished rice can be absorbed and utilized more quickly than half-polished or unpolished rice. They think it possible that there may be a greater absorption of carbohydrates from the intestine than that suggested by SUGIMOTO. Unabsorbed carbohydrates may be disintegrated by the intestinal bacteria, which would account for the differences in the respiratory metabolism in different grades of polishing.

W. P. B–S.

VAN BERKHOUT (P. J. Teding). **Microbiological Investigation as to the Extent to which Rice has been polished.**—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1926. Pt. 4. pp. 489–502. [35 refs.]

The importance of discovering a method for the standardization of rice was recognized by the 6th Congress of Far Eastern Association of Tropical Medicine which met in Tokyo in 1925. No method has so far proved to be satisfactory. By means of microbiological methods the author sought to determine how far the growth of yeasts was stimulated by rice extracts, and it was shown that yeast grows more quickly in the presence of bran vitamin-holding extracts than without. These extracts stimulated not only the growth but also fermentation of the yeast, but the increase of fermentation was variable and was not found to be proportionate to the quantity of bran. After much work

on these lines the author concludes that there are indications that this method might be useful for estimating the degree of polishing to which rice has been subjected.

P. W. B–S.

SHIMAMURA (Torai) & NAITO (Kan). **Experimental Studies on the Effects of Polished Rice Feeding and its Vitamin-B Defect in the Horse.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress Toyko, 1925.* Vol. 1. pp. 249–252.

Korean ponies were fed on polished rice and boiled rice straw. In from 4 to 12 months there was loss of appetite and body weight, pulse increased in rate and irregular, with paralysis of the hind legs; no rise in temperature nor intestinal symptom. The course was acute. Some of the symptoms coincided with those of human beriberi.

P. W. B–S.

SUGIMOTO (K.), YASUDA (Y.) & KAKEGAWA (S.). **On the Variations of Several Substances in the Different Organs and Blood of Fowls kept on Polished Rice.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 279–282.

The heart, liver, muscles, bone and blood of fowls of about 1,500 gm. weight were examined. Half of those fed upon unpolished rice gained weight. The organs of those fed upon polished rice appeared to lose weight, and in these birds there was a small increase of acetone bodies in the blood. Sugar appeared when symptoms of beriberi were present. Generally in fasting birds glycogen in the liver is a little decreased; when polyneuritis appeared the loss of liver glycogen was great.

P. W. B–S.

SUZUKI (Tadashi). **Studies in the Vitamine B-Content (Rat-Growth-Promoting Water-Soluble B.) in the Mother's Milk of Infants suffering from Infant-Beriberi.**—*Oriental Jl. Dis. Infants.* 1926. Apr.–July. Vol. 1. No. 2 & 3. English summary. pp. 51–72. With 9 charts and 18 figs. on 4 plates. [In Japanese.]

The author gives a very clear and detailed description of his experiment on rats, in which he shows that the milk of beriberi mothers when given in an amount of 2 cc. daily has no power to cure avitaminosis in rats, but that a vitamin extract "oryzanin" immediately cures these cases if the animal is not too far gone. This amount of beriberi milk not only failed to cure the rats, but increased their symptoms. It was, however, evident that the vitamin B was not entirely absent, for if 4 cc. were given the diseased rats often recovered and this quantity was preventive. The experiments incidentally disprove the presence of any toxin in the beriberi milk. The author carefully states that though beriberi milk is deficient in vitamin B, we cannot therefore assert that beriberi is caused by avitaminosis because in beriberi hypertrophy of the heart is always found, whereas it is not so in avitaminosis.

P. W. B–S

Suzuki (Tadashi). **Studies in the Vitamine-Content (the Yeast Growth-Promoting Stimulus) of Mother's Milk whose Infants are suffering from Infant-Beriberi.**—*Oriental Jl. Dis. Infants.* 1927. Jan. Vol. 2. No. 1. English summary pp. 113–117. [In Japanese.]

Eighteen specimens of milk taken from beriberi cases contained similar yeast growth-promoting stimulus to that found in milk in other acute diseases and certain chronic conditions, but less than that found in Oryzanin. The author therefore concludes that this indicates the amount of the water soluble vitamin B in beriberi milk. He is unable to explain infantile beriberi as a simple avitaminosis.

P. W. B–S.

Okada (Seizaburo) & Sakurai (Eiichi). **The Basal Metabolism in Beriberi.**—*Arch. Intern. Med.* 1926. Dec. 15. Vol. 38. No. 6. pp. 770–778. [2 refs.]

Little research has been done upon the basal metabolism of beriberi except by the authors. Fleming examined one case, but found no essential alteration in the disease.

The authors' conclusions are— (1) In most cases of beriberi quite normal values in basal metabolism and the respiratory quotient were found. (2) With threatened cardiac incompetency an increase was observed. (3) When paralysis and atrophy were very marked a diminution in the basal metabolism was noted.

P. W. B–S.

Jansen (B. C. P.) & Donath (W. F.). Over de isoleering van het anti-beriberi vitamine. [**On the Isolation of the Anti-Beriberi-Vitamin.**] —*Geneesk. Tijdschr. v. Nederl. Indië.* 1926. Vol. 66. No. 6. pp. 810–827. With 5 figs. on 2 plates. [20 refs.]

A summary of the preliminary report on this subject has been given (*ante*, p. 126). The various stages of the isolation of the vitamin are given here in detail, which should be consulted in the original by those interested. In a postscript the authors point out that the preparation of the pure vitamin is far too expensive for practical purposes. The comparatively simple structure of the substance, however, is promising in regard to the possibility of its synthetical preparation. In the meantime they propose the therapeutical application of one of the intermediate products (acid clay, activated by the adsorption of the vitamin), which they call "actamin." It is said to be a stable substance, cheap enough for practical purposes.

W. J. Bais.

i. Yabe (Seinosuke & Endo (Nichiro). **Experimental Prophylaxis and Therapy of Pigeon's White Rice Disease with the Juice of "Natsumikan" Orange.**]—*Saikingaku Zasshi* (*Jl. of Bact.*) 1926. Feb. No. 360. [Summarized in *Japan Med. World.* 1926. Nov. 15. Vol. 6. No. 11. p. 324.]

ii. – – – . **On my Orange ("Natsumikan") Cure of Beriberi.** – *Ibid.* [*Japan Med. World.* p. 324.]

i. The authors report that by giving 16 cc. of fresh orange juice the experimental disease of pigeons was cured and that it also acted as a prophylactic. Heating the juice to 100° C. did not reduce its efficacy.

ii. The authors state that orange juice was useful as a therapeutic agent in beriberi.

P. W. B–S.

Fujinami (Akira). Historical Review of Research on Kakke in Japan.—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 11–17.

Hara (Tetsuichi), Takada (Ryohei) & Matsumuro (Hideo). On the Utilization of Rice Polishings.—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 245–247.

Irisawa (Tatsukichi) & Sakamoto (Tsuneo). Ueber die Beziehung zwischen B-Avitaminose und Beriberi.—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 205–209.

Jansen (B. C. P.) & Donath (W. F.). Isolation of Anti-Beriberi-Vitamin.—*Meded. Dienst d. Volksgezondheid in Nederl.-Indië.* 1927. Pt. 1. pp. 186–199. With 6 figs. on 3 plates. [Refs. in footnotes.]

Ogata (Tomosaburo). Zur Frage nach der Avitaminosentheorie der menschlichen Beriberi.—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo,* 1925. Vol. 1. pp. 19–24. [15 refs.]

Okada (Seizaburo). Basal Metabolism and Vital Capacity in Beriberi.—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 211–212. [2 refs.]

Plummer (Beulah A.). The Motility of the Intestinal Tract in Experimental Beriberi (Rats) and Scurvy (Guinea Pigs).—*Amer. Jl. Physiol.* 1927. Apr. 1. Vol. 80. No. 2. pp. 278–287. [11 refs.]

Shiga (K.). Prophylaxis of Kakke (Beriberi) and on Kakke of Chosenese.—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 213–221.

Shirabe (Michitaro). Die Ursache von Beriberi.—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 227–231.

Takahira (Hideo) & Ishibashi (Eiichi). Metabolism of Fowls kept on Normal Food, Fasting, Polished Rice and Vitamin-B Deficient Food.—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 1. pp. 239–243.

UNDULANT FEVER.

Hull (Thomas G.) & Black (Luther A.). **Undulant Fever as a Public Health Problem.**—*Jl. Amer. Med. Assoc.* 1927. Feb. 12. Vol. 88. No. 7. pp. 463–464. [10 refs.]

The authors state that the infectivity of *Br. abortus* to man was first proved by Keefer in 1924 ; since then cases have been reported (1) by Evans ; (1) by Duncan ; (3) by Huddleston, and (7) by Carpenter. Sixty-nine sera sent to the laboratory for Widal test were tested with *Br. abortus* ; 5 gave agglutination at 1/200, 1 at 1/50, and 5 at 1/25. The fact that many persons have agglutinins in their serum for *Br. abortus* was shown by Sedgwick in America. Evans considers 1 in 20 suggestive, the authors 1 in 50. As there are practically no goats in Illinois they can be ruled out ; cattle and hogs would be possible sources, cattle the most probable.

P. W. Bassett-Smith.

Lim (C. E.). **Isolation of *M. melitensis* from Patients in China.** (Abstract.)—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 2. pp. 763–764.

The author reports that there is no authentic record in cases of undulant fever in China of the diagnosis having been made by isolation of the specific organism or specific agglutination. He describes an epidemic among Sikh watchmen of a coal mining company at Chiaotso, Honan. These were from the Punjab. In 1924 four cases occurred, recognized clinically and by agglutination (1/400–1/600). The Sikhs kept a small herd of Chinese goats for milk. Was the disease introduced from the Punjab to the goats by "carriers"? Since the goats were quickly destroyed this cannot be determined. It is stated that a small outbreak followed the arrival of new watchmen from the Punjab. The Micrococcus was obtained from the blood of one. No cases occurred among the Chinese.

The author holds the view that text books are in error when they state that undulant fever is endemic in the Yangtse area, but it must be remembered that an increasing quantity of goat's milk is used by foreigners and "carriers" are possibly present. A survey of the incidence of infection among the native goats is desirable.

P. W. B-S.

Raynaud (Lucien). La fièvre ondulante en Algérie. [**Undulant Fever in Algeria.**]—*Bull. Office Internat. d'Hyg. Publique.* 1926. Dec. Vol. 18. No. 12. pp. 1405–1408. With 1 map. [4 refs.]

In 1907 there was a small epidemic of undulant fever at Kleber, Prov. of Oran, which was traced to the local goats ; since that time there had only been sporadic cases until 1926 when the following were noted : January (1) ; March (6) ; April (6) ; May (19) ; and June (30) cases, in all 62 cases increased to 74 by July 9. In the infected region goat's milk is almost exclusively used by a population largely Spanish. Each day from 5 to 6 thousand litres of this milk are drunk or an annual total of two and a half million litres. The municipality of Oran ordered that all milk should be boiled and recommendations with regard to the herds of goats were issued, but there is no power to enforce them. At

Sidi-Chumi, where 4 cases had been noted among the goat herds, 7 per cent. of the milks were infected.

In Algeria there is little evidence of epidemic abortion in the cattle.

P. W. B-S.

Ardin-Delteil. Sur la diminution de fréquence de la fièvre ondulante en Algérie et dans notre sphère d'observation. [**Reduction of Undulant Fever in Algeria.**] —*Arch. Inst. Pasteur d'Algérie.* 1926. Sept. Vol. 4. No. 3. pp. 457–469.

The author shows that since 1895 infection of men and goats with *M. melitensis* has been fairly common in Algeria. In 1911–25 out of 9,806 analyses made in the Pasteur Institute, however, there were only 83 positive reactions, or an average of 5·9 cases per year. The disease has not made any great extension since 1919, being chiefly present in the province of Oran. This is probably due to the fact that in 1908 the importation of Maltese goats was stopped. Details of the cases in the different provinces are given in full.

P. W. B-S.

Béguet (M.) & Torstenson (H.). La fièvre ondulante dans la région oranaise en 1926. [**Undulant Fever in Oran District in 1926.**]—*Arch. Inst. Pasteur d'Algérie.* 1926. Sept. Vol. 4. No. 3. pp. 470–472. [6 refs.]

The authors show that the centres of undulant fever in Oran district are now few, owing to the prophylactic measures taken ; but it is still maintained by infected Spanish goats.

P. W. B-S.

Torstenson (Harald). Recherches sur les animaux domestiques porteurs de *M. melitensis*, autres que la chèvre. [**Search for Carriers of *M. melitensis* in Domestic Animals other than the Goat.**]—*Arch. Inst. Pasteur de Tunis.* 1926. Dec. Vol. 15. No. 4. pp. 305–308. [2 refs.]

Many workers have found that various animals are susceptible to infection in the laboratory with *M. melitensis*. The author has carried out researches to see if some of these are infected naturally. He tested dogs, cats, rabbits, fowls, wild rats and guineapigs, all of which were taken from goat stables, houses of goatherds and other places in close association with the goats. The almost consistently negative results tend to show that besides goats (and sheep) there are practically no domestic animals naturally infected with *M. melitensis* in Tunis, but he states that no researches have been made on cattle and pigs.

P. W. B-S.

Torstenson (H.). Sérodiagnostic de la fièvre ondulante négatif chez des moutons algériens. [**Algerian Sheep Negative to Serum Test for Undulant Fever.**]—*Arch. Inst. Pasteur d'Algérie.* 1926. Sept. Vol. 4. No. 3. p. 473.

The author has tested the blood of 208 Algerian sheep with *M. melitensis*, *M. para-melitensis* and *B. abortus* without finding any evidence of infection.

P. W. B-S.

Vidal Munné (José). El aborto epizoótico y sus relaciones con la fiebre de Malta del hombre (Trabajo premiado por la Real Academia de Medicina y Cirugia de Barcelona). [**Contagious Abortion and its Relation to Undulant Fever in Man.**]—*Rev. Hig. y Sanidad Pecuarias.* 1927. Apr. Vol. 17. No. 4. pp. 265–281. [97 refs.]

This article is a review of the relations of *B. abortus* and *M. melitensis*, and thus consists chiefly of a summary of views put forward in the last few years. The author regards milk as a very important vehicle of infection with *B. abortus*, and states that the majority of cases of undulant fever in man where no caprine source can be found may be due to the contaminated milk of cows and, in a later section, that undulant fever is an enzootic which may affect animals and man; thirdly, that there is no valid method at present known of distinguishing the two organisms, the bacillus isolated by haemoculture from man or goats being designated *B. melitensis*, while, if isolated from the cow or other animal, it is called *B. abortus*.

From 90 cases whose sera agglutinated in a titre of over 1 : 200, the highest being 1 : 10,000, he found :—

Sera agglutinating in equal titre *B. melitensis* and *B. abortus*	41 or 45·5 per cent.
Sera agglutinating *B. melitensis* in higher dilution	11 or 12·2 per cent.
Sera agglutinating *B. abortus* in higher dilution ...	16 or 17·7 per cent.
Sera agglutinating *B. melitensis* only	11 or 12·2 per cent.
Sera agglutinating *B. abortus* only	11 or 12·2 per cent.

He also examined the sera of 256 cows killed at the slaughter-house of Barcelona and found 35·15 per cent. which agglutinated " la brucella " [? *B. melitensis*] in a dilution of over 1:200, a close approximation to the figures of Stuart (*Trans. Roy. Soc. Trop. Med. & Hyg.* June, 1925), where 31·2 per cent. of 542 sera examined agglutinated the *B. abortus*.

He has repeated the experiments of Vercellana & Zanzucchi on non-specific agglutination, but thinks that this method is valueless for differentiation of the organisms. [this *Bulletin*, Vol. 23, p. 729; *ante*, p. 112]. A good and fairly comprehensive bibliography is appended.

[It is remarkable that in 24 per cent. of the 90 cases (presumably human) there were present no group reactions, 12 per cent. reacting only to Melitensis and 12 to Abortus; this in itself is a rather important fact and suggests some differential character which should be followed up. Bovine infection with Melitensis from goats has long been known and is not necessarily the same as Abortus infection.—P. W. B-S.].

H. Harold Scott.

Evans (Alice C.). **Human Infections with Organism of Contagious Abortion of Cattle and Hogs.**—*Jl. Amer. Med. Assoc.* 1927. Feb. 26. Vol. 88. No. 9. pp. 630–632. [14 refs.]

This is largely a résumé of what has already been published, but Miss Evans is more dogmatic than some would think warranted. " The disease in man contracted from cattle and hogs is indistinguishable clinically from that prevalent in the Mediterranean countries and known as Mediterranean or Malta fever." The paper is, however, very valuable and should extend the search for these cases.

She reports 20 described cases of supposed bovine and porcine origin; many are attributed to the consumption of unboiled milk [but often

not proved'. The South African cases are referred to, and the increased frequency in Italy, ascribed to cows' milk, as well as a case reported from Palestine and possibly others in the Dutch East Indies.

P. W. B-S.

Bamforth (J.). **Two Cases of Undulant Fever occurring in England.**—*Lancet.* 1927. Apr. 16. pp. 818–819. With 2 text figs. 1 ref.

The author reports two cases of prolonged fever of an undulant type which occurred in patients, one of whom had never been out of England, and one only in France during the war. The former was a woman aged 63 of Essex, the second a man of Kent, aged 40. In both these cases the blood agglutinated *M. melitensis* to 1 in 1,000 and *B. abortus* to 1 in 2,000. No blood culture was obtained. Both patients had drunk cow's milk, but never goat's milk. In the absence of further bacteriological information it is impossible to say whether they were suffering from abortus or melitensis infection, but the author states that the higher agglutination to *B. abortus* points to its being the causative organism.

[It will be noted that both were isolated cases in country districts, which is rather against a milk infection from cows.]

P. W. B-S.

Warren (C. W.), Smith (Glen) & Lindner (Max B.). **Undulant (Malta) Fever, with Report of Two Cases.**—*Clifton Med. Bull.* 1926. Dec. Vol. 12. No. 4. pp. 125–130. With 4 text figs. [7 refs.]

The authors report two cases treated in hospital in New York and thought at first to have been enteric. They were finally considered to have been undulant fever, for the blood of both agglutinated *Br. melitensis* and *Br. abortus* in high dilution ; the blood cultures, however, were all negative. No definite source of infection could be traced, since all milk tested gave negative reactions, and there was no evidence of recent abortion in the cattle of the farm. It must be noted that in both these cases agglutination for typhoid was positive in dilutions of 1/80–1/40.

[There appears to be little justification for the diagnosis " undulant fever cases caused by *Br. abortus*."]

P. W. B-S.

Duffie (H.). **Undulant (Malta) Fever : Two Fatal Cases in Michigan.**—*Jl. Amer. Med. Assoc.* 1926. Nov. 27. Vol. 87. No. 22. pp. 1830–1831.

A farmer of Michigan, with his wife and three children, occupying a house which had been long disused, contracted what they thought was influenza. A boy aged six had high fever, temperature 106°, nephritis and cough, with a high leucocyte count ; he became lethargic and died. The post-mortem showed pleuro-pneumonia.

The father and mother also developed high fever with sweats, delirium and vomiting or diarrhoea. The man had abundant rose spots in successive crops and orchitis. The woman developed temporary

glycosuria. Blood cultures and examination of the stools for *B. typhosus* were negative, but the blood agglutinated *B. abortus* to 1 in 40. There were symptoms of pulmonary consolidation and death in a fortnight.

The post-mortem showed no evidence of typhoid ; the spleen in the woman was twice normal size, that of the man was normal.

Dr. HUDDLESTON, of the Michigan State College, diagnosed the cases as *B. abortus* infections. The horses at the time were suffering from distemper.

[The title of this paper is unfortunate and misleading, for though there was a low agglutination reaction with *B. abortus*, the clinical symptoms and the post-mortem signs are not those of undulant fever, as we know them ; whatever the author's opinion may be of the morphological unity of the organisms, to call the cases Malta or undulant fever only serves to perpetuate the present confusion relating to this disease. There were three deaths, not two, if we include that of the boy, and no specific organisms were isolated to corroborate the diagnosis.]

P. W. B-S.

FRISE (W.), SDRODOWSKII (P.) & MINERVIN (S.). Trois cas de contagion de laboratoire causée par le microbe de la fièvre méditerranéenne. [**Three Cases of Laboratory Contagion of Undulant Fever.**]—*Russian Jl. Trop. Med.* 1926. No. 9–10. French summary p. 30. [In Russian pp. 29–30.]

These cases varied in severity from the acute typhoid type to an ambulant form. The diagnosis was confirmed by blood cultures, agglutination and by complemental fixation methods.

P. W. B-S.

MAZZUCCONI (M.). Sulle lesioni determinate dall'infezione sperimentale da " Micrococcus Melitensis " sull'occhio. [**Ocular Lesions caused by Experimental Infection by** *M. melitensis*.]—*Ann. di Med. Nav. e Colon.* 1927. Jan.–Feb. Year 33. Vol. 1. No. 1–2. pp. 14–22. [8 refs.]

MORELLI in 1925–6 recorded the effects of inoculation with two strains of *Brucella melitensis* of the cornea of rabbits after scarification, of injection into the anterior chamber, and into the vitreous. These the author repeated, and confirmed the lesions of the cornea and iris recorded by MORELLI. He found also that similar effects were produced by using material directly from a previously infected rabbit and, thirdly, tested the effects of infected material from animals and a pure culture on the intact conjunctiva. By injection not only were similar lesions produced, but the infective agent acquired an enhanced virulence. Lachrymation and photophobia, followed by purulent conjunctivitis and the development of small punctate granulations occurred. These extended and fused, setting up a widespread keratitis and iritis, and the cornea became opaque. Some 12 days subsequent to inoculation the condition began to clear up, and in a fortnight more, except for residual adhesions of the iris, the animals appeared well. Serum tests gave variable results. In one case, agglutination was positive in a dilution of 1 : 800, in another it was feeble, in a third negative. The organism had no effect on the intact conjunctiva, as MORELLI had previously found. [DE GASPERI,

this *Bulletin*, Vol. 23, p. 359, found that there were irregular results with rabbits but plastic iritis was generally caused. The inoculation was of no use for differentiating *B. melitensis* from *abortus*.—P. W. B-S.]

H. Harold Scott.

Giuffrè (M.). Osservazioni sulla vaccinoterapia nella febbre mediterranea. **Vaccine Therapy in Undulant Fever.**—*Pediatria.* 1927. Apr. 1. Vol. 35. No. 7. pp. 345–358. With 6 charts in text. [44 refs.]

Nine cases of undulant fever treated by injections of vaccines are described. In some the diagnosis was made by haemoculture, in others by agglutination tests. The effects of the injections were remarkable. In many there was a crisis within a few hours, and in all there was an early amelioration of the general condition. Good results were obtained when the vaccine was administered intramuscularly, but better still when the intravenous route was employed. There was generally a systemic reaction with access of fever, and at times a focal reaction. One case with somewhat anomalous symptoms did not react like the others, and this is regarded as one of mixed typhoid and undulant fever, because the serum agglutinated *B. typhosus* in a dilution of 1 : 100, and *B. melitensis* 1 : 500 ; blood-culture was negative.

[There is no record of doses given in this rather remarkable series of cases and the rapid results would appear to be " Shock " reactions.—P. W. B-S.]

H. Harold Scott.

Evans (Alice C.). **Studies on** *Brucella* (*Alkaligenes*) *melitensis*.—*U.S. Pub. Health Service. Hygienic Laboratory Bull. No. 143.* 1925. Aug. 67 pp. With 2 charts & 1 plate. 1925. Washington.

This bulletin has five separate parts and a bibliography. Four of these, previously published in the *Public Health Reports* during 1923–24, have been amended and the fifth added under the heading " Hogs as a possible source of human infection." The author divides the strains examined into eight groups, three of which contain only one specimen. The others are : (1) The largest group, mostly of animal origin, var. *abortus*, five human out of 33 ; of these five, four at least were isolated from American cases ; (2) var. *para-abortus*. Human and goat origin, from north Africa and Sicily ; (3) var. *melitensis A.*, mostly human, from Western and Eastern sources ; (4) var. *melitensis B.*, all from Malta and N. Africa, human and caprine ; it is notable that this group is most closely allied morphologically and serologically with the original *M. melitensis* types ; (5) var. *paramelitensis*, all from Malta and Tunis. A plate is given which clearly demonstrates the marked coccus-like character of the three most important types. Many of the strains tested had been long under subculture, which with the variations of animals through which the organism has passed may well give rise to changes in character of the reactions.

Part 5. It is demonstrated that infection can be contracted by handling carcasses of hogs, and that the organism when isolated is more virulent than that from cows. All but one of the cases were from the Western hemisphere, where the infection is on the increase. This, with the fact that cases in France are attributed to handling sheep carcases,

renders it necessary to be very much on the alert for the disease in butchers and others who handle the dead animals or their skins (and to notify the same as human abortus infections.)

P. W. B-S.

Sanfilippo (Emanuele). Sulla immunizzazione antimelitense. [**Immunization against Melitensis Infection.**]—*Biochim. e Terap. Sperim.* 1926. Nov. 30. Vol. 13. No. 11. pp. 426–440. [1 ref.]

By prolonged series of experiments performed with mice and white rats it was demonstrated that the latter are less sensitive to the toxin of *M. melitensis*. Cultures of the organism were killed by heating to 60° C. for 2–4 hours or by contact with chloride of gold.

Injection was made intraperitoneally. The rats survived after as much as 8 such agar-cultures and presented merely temporary loss of weight, but 10 cultures in some rats proved fatal, with rapid loss of weight leading to marked cachexia if death did not occur in the first three or four days. Autopsy revealed hyperaemia of the peritoneum and internal organs, and subpleural petechial haemorrhages.

The vaccine resulted in the production of feeble agglutinating powers in the serum, 1 : 20–1 : 75 only, ten days after inoculation.

In the experiments on immunization, a week after vaccination the animals were inoculated with four times the lethal dose of virulent cocci. If they lived they showed evidence of infection ; if death occurred cultures could be obtained from the spleen, the medulla of the bones, the lymphatic glands and the kidneys, but none from the liver. None of the rats, after vaccination with 4 cc. (i.e. 8 cultures prior to emulsion) of the killed organisms, showed any symptoms worth noting on subsequently receiving 4 lethal doses of the virulent cocci. Comparing the results in white rats with those in mice, it was found that the lower sensitiveness of the former corresponded with the development of a lower degree of immunity.

A second series of experiments was performed, substituting oral administration of the virulent organism for the intraperitoneal route. Two to four agar cultures were given on bread dipped in milk. The results proved to be the same as with the former method.

The author's conclusions may be summed up as follows :—

1. The rat is less sensitive than the mouse to the toxin of the micrococcus, but presents considerable individual variations of sensitiveness.
2. The rat can be actively immunized against undulant fever by intraperitoneal or oral administrations of vaccine.
3. Being less susceptible than the mouse to cultures killed by heat it is not necessary to use organisms killed by chloride of gold, as is needed with the latter.
4. The protection conferred by vaccination with cocci killed by either method is specific, but is of greater degree in mice than in white rats.

H. Harold Scott.

Ascoli (Maurizio) & Sanfilippo (E.). **On the Immunization of the Goat against Undulant Fever.**—*Jl. Trop. Med. & Hyg.* 1927. Jan. 15. Vol. 30. No. 2. pp. 19–21. [13 refs.]

Following the work of Vincent many, not very successful, attempts have been made to immunize goats. Recently the authors have again

taken up the subject and have inoculated two goats, one with culture killed by heat, the other with a culture killed and precipitated with gold chloride, which frees it from toxicity. The animals afterwards received by the mouth large doses of a living highly-virulent culture. The results were unexpectedly satisfactory, the animals showed no symptoms and the organism could not be recovered from the goats after death, while the control was heavily infected, the organs giving abundant subcultures. The length of the immunity, however, has not been determined. The gold killed vaccine is said to be better tolerated and to give higher agglutination titre.

P. W. B-S.

Graziosi (A.). Sulla agglutinazione aspecifica con acido lattico per differenziare il bacillo di Bang dal *Micrococco melitense*. [**Non-Specific Agglutination by Lactic Acid as a Means of distinguishing** *M. melitensis* **from** *B. abortus*.] —*Nuovo Veterinaria*. 1926. Nov. 15. Vol. 4. No. 11. pp. 306–309.

After quoting previous reports on the value of this test, the author repeated it with 8 strains of *M. melitensis* and 10 of *B. abortus*. Of the former only two strains were agglutinated by dilutions of 1 : 500 or over, and two were not agglutinated at all. Three only of the ten strains of *B. abortus* were not agglutinated even in very low dilutions. Vercellana and Zanzucchi had come to the conclusion that *M. melitensis* is always agglutinable by a dilution higher than 1 : 300, while *B. abortus* proved negative.

With this the author's results do not agree, and in his opinion, therefore, the test is quite unsafe as a diagnostic criterion.

H. Harold Scott.

Sangiorgi (Giuseppe). Sulla questione della differenziazione del " B. abortus " dal " M. melitensis " e sul valore per le " Brucelle " del saggio di agglutinazione aspecifica mediante l'ac. lattico. [**The Differentiation of** *B. abortus* **from** *M. melitensis* **by Means of Non-Specific Agglutination with Lactic Acid.**]—*Pathologica*. 1927. Jan. 15. Vol. 19. No. 423. pp. 3–6.

This paper is of interest in presenting a condensed summary of the vexed question as to the identity or otherwise of *M. melitensis* and *B. abortus*. The author first states the claims of the unicist and the dualist, some basing their conclusions on laboratory methods, others on epidemiological, others again on clinical grounds. It is suggested that there may be variations, mutations, and adaptations. Thus, as Bastai holds, there is a bovine abortion due to *M. melitensis* able also to infect man, besides abortion due to *B. abortus*, non-infective for man. The six laboratory tests are mentioned, namely, the relative thermostability of *B. abortus* as compared with *M. melitensis* (Ficai & Alessandrini); the failure of anti-abortus serum to agglutinate an emulsion of *M. melitensis* in bile (Domingo); the anaphylactic test (Polettini); the better growth and greater production of alkali in peptone-water media with organic salts (Brown, Duncan & Henry); the differential staining methods of Bezssonoff; and lastly, the non-specific agglutination by lactic acid in dilutions of 1 : 300 and over (Vercellana & Zanzucchi).

The discordant results recorded of the last are due possibly to different sources of the strains employed. The test should be regarded as valid only when the *B. abortus* used has been isolated from animals and in regions where undulant fever in man is unknown, and, *mutatis mutandis*, with *M. melitensis*.

It is suggested that as there is a *B. paramelitensis*, or strain of *melitensis* non-agglutinable with anti-melitensis serum, so there may be an analogous *B. para-abortus*.

H. Harold Scott.

Enrico (Cesare). La resistenza al calore delle agglutinine antibang e antimelitense. [**The Thermoresistance of Agglutinins of** *B. abortus* **and** *M. melitensis*.]—*Ann. d'Igiene.* 1926. Dec. Vol. 36. No. 12. pp. 825–841. [40 refs.]

The author, having noted the discordant results reported by those who had made trial of Ficai and Alessandrini's method of differentiating *B. abortus* from *M. melitensis*, repeated the tests with immune sera obtained by experimental inoculation of various animals, guineapigs, rabbits, sheep, and white rats. Monkeys were also tried, but no agglutinating serum was obtained from these. The results are unfortunately not satisfactory; either the differences were so slight as to be valueless, as in the cases of guineapigs and rabbits; or varied in different individuals of the same species, as in the white rats; or no agglutinins were produced at all, as in the monkeys.

Diversity of reported results, it is suggested, may be due to experimental infection differing from the natural as to the production of agglutinins.

H. Harold Scott.

Béguet. Sur les conditions de l'agglutinabilité des microbes et du phénomène de l'agglutination (étude faite sur *Br. melitensis* et *Br. abortus*. [**Conditions of Agglutinability of Microbes:** *Br. melitensis* **and** *Br. abortus*.]—*Ann. Inst. Pasteur.* 1927. Jan. Vol. 41. No. 1. pp. 49–58. [6 refs.]

The author has shown that the phenomenon of agglutination of suspensions of microbes is due to the flocculation of different bacterial substances, part adsorbed upon the bodies of the microbes and part diffused in the liquid. This flocculation depends upon variations in concentration of the substances, the temperature, and the ionization of the liquid of the suspension, and these are governed by the general laws of the stability of colloidal solutions. With regard to *Br. melitensis* there is. (1). A substance flocculable by heat in saline solutions, by acids, and by non-specific serums which can be removed by adsorption with charcoal. This substance appears to be a surface product of the microbe (Burnet). (2). A substance flocculable by salts which is easily demonstrated after the first has been removed. (3). A substance flocculable by specific serum, purely bacterial and specific to the genus *Brucella*. The flocculation of this substance is hindered by a high concentration of the heat flocculable body. This hypothesis reconciles the different hypotheses of Paltauf, Nicolle & Bordet.

P. W. B-S.

Tapia (Manuel) & Martin de Nicolas (Arturo). Sobre la posible diferenciación serológica entre el *Micrococcus melitensis* de Bruce y el *Bacillus abortus* de Bang. [**On the Possibility of differentiating Serologically** *M. melitensis* **from** *B. abortus.*]—*Arch. Inst. Nac. Higiene de Alfonso XIII.* 1926. Oct. Vol. 4. No. 4. pp. 39–71. [18 refs.]

The first part of this valuable paper briefly reviews and summarizes the work of Evans, Khaled, and Potellini in the different aspects of their investigations. After this very useful summary the authors relate their own experiments. They used sera from human undulant fever patients, the sera of commerce, sera obtained from the horse and the goat, and those prepared experimentally from rabbits, guineapigs, sheep, and man.

Their first group of agglutination experiments was performed with heated sera, the readings being taken after the mixture had been kept at 37° C. for two hours, and then at room-temperature for 24 hours.

These experiments were carried out in different series, using the sera from the various sources named above. The results of each test are given in a number of tables, which save much writing. It is shown that with serum from the horse, goat and sheep, the findings of Ficai and Alessandrini were not confirmed, In the case of the former two, for example, agglutinins, both specific and non-specific, are destroyed by heating to 65° C.

With a second series, employing six human sera, five of these lost the power of agglutinating after being heated to 65° C.; only one retained it.

Again, a guineapig, immunized with *M. melitensis*, was subsequently immunized with *B. abortus*. The only effect noticed was a *lowering* of the agglutinating titre of the serum against both organisms.

All the experiments performed cannot be detailed, the original may be consulted with advantage; the following, however, are the well-considered conclusions drawn by them:—

1. By agglutination only the differences are insufficient to place the organisms of undulant fever and contagious abortion in two species. The authors' results differ from those of Evans, of Khaled, and of Potellini, in each of the conclusions of these authors.

2. Using heated serum gives no more useful data than the simple agglutination. It is true that certain differences do exist in the titre of agglutination, but these differences are no greater between the effects on the two organisisms than between the effects of sera from different animals on the same organisms.

3. Heating by the methods of Negre, Raynaud, and Finzi does not destroy the agglutinating power.

4. The discordant results recorded by investigators are doubtless due to different strains of organisms employed, both of *M. melitensis* and of *B. abortus*.

A second series of experiments was carried out using saturated and heated sera, but very discordant and irregular results were obtained. These are given, as with the previous tests, in tabular form, and the authors state that owing to the inconstancy of results no reliable deductions can be drawn.

H. Harold Scott.

Huddleson (I. Forest), Hasley (D. E.) & Torrey (J. P.). **Further Studies on the Isolation and Cultivation of *Bacterium abortus* (Bang.)**—*Jl. Infect. Dis.* 1927. Feb. Vol. 40. No. 2. pp. 352–368. [27 refs.]

It has been previously reported that the primary isolation of *B. abortus* generally requires definite peculiarities for success, e.g., an increased CO_2 content. In this work the method has been very fully developed and it appears that in the growth of the organism three biological reactions may occur.—(1). Production of CO_2 which gradually reaches a point which is the optimum for the organism. (2). Production of H_2S from sulphur containing amino-acids. (3). The formation of ammonium magnesium phosphates in alkaline media when ammonia from the amino-acids comes in contact with magnesium phosphates. Incidentally the amount of H_2S given off, detected by lead acetate papers in the tube, is said to be diagnostic between abortus and melitensis. After much work in isolation of the *B. abortus* from various substances and tissues the very important fact is fully demonstrated that for the detection in milk, it is not the centrifuged deposit that is most reliable for culture but the cream, since the cells and bacteria are carried up. Culture of this on special media is more satisfactory than animal experiment, being more practical and rapid. This infection of the cream must have a very important effect on prophylactic measures. The paper is very full of detail and should be read in extenso by those interested in the subject.

P. W. B-S.

Bua (Francesco). Sui rapporti tra melitensis ed abortus. L'intradermoreazione nella melitense con antigene-abortus. [**The Relations between *B. melitensis* and *B. abortus*. Intradermal Reaction in Melitensis Infection with Abortus-Antigen.**]—*Policlinico.* Sez. Prat. 1927. May 2. Vol. 34. No. 18. pp. 631–635. [21 refs.]

The author used for the intradermal test cultures of the organisms, a loopful emulsified in 2 cc. of normal saline, sterilized by heat and carbolized (0·5 per cent.). He tested the abortus antigen in 5 cases of undulant fever, and 51 of other diseases, tuberculosis, paratyphoid B., pneumonia, malignant disease, etc., and obtained positive results identical with those from *B. melitensis* antigen in the five cases, but negative in the others.

H. Harold Scott.

Messieri (A.). Studio sperimentale sull' infezione da germi del genere "Brucella" nella specie canina. [**Experiments on Infection of Dogs by the Brucella Group of Organisms.**]—*Nuova Veterinaria.* 1926. Dec. 15. Vol. 4. No. 12. pp. 317–325. With 2 text figs. [4 refs.]

The dog has for a long time been regarded as resistant to *M. melitensis*. To test the matter three series of experiments were undertaken. Emulsions were made: (1) of the spleen of guinea-pigs infected with *M. melitensis* obtained from a goat; (2) with the same organism from a human case; and (3) with *B. abortus* recently isolated from a foetal calf.

The conclusions given are these :—

1. Healthy dogs are very resistant to experimental infection with *M. melitensis* and *B. abortus* and large amounts must be used.
2. The time of stay of the organism in the infected dog is relatively short.
3. No pathological difference can be made out between the effects produced by the two organisms.
4. Healthy dogs placed in contact with those infected (e.g., pups born of infected mothers) do not contract the disease.
5. Experimental infection did not generally determine abortion except in an advanced stage of the pregnancy.

[Dogs have frequently been known to be naturally infected in Corsica and India.—P. W. B-S.].

H. Harold Scott.

Huddleson (I. Forest) & Winter (O. B.). **Magnesium Ammonium Phosphate Crystals in Aerobic Cultures of** *Brucella abortus* **and** *Brucella melitensis*.—*Jl. Infect. Dis.* 1927. Apr. Vol. 40. No. 4. pp. 476–478. [3 refs.]

The authors have noted the occurrence of magnesium ammonium phosphate crystals in the special liver medium when cultures of *Br. abortus* and *Br. melitensis* are grown aerobically in it. It is now shown that the large size of the crystals is due to their slow formation in a semi-solid medium. The increase in the pH of the medium and the separation of the crystals are due to the formation of ammonia, produced by the activity of the organisms in the culture medium and the formation of the salt interferes with their viability. Old strains of both differ markedly in their ability to cause the formation of the salt ; the strains have to be frequently subcultured to retain their viability when grown aerobically. Similar crystals may be produced in the media artificially in the absence of the organisms.

P. W. B-S.

Izar (G.) & Mastrojeni (G.). Sulla chemioterapia della infezione melitense. [**Chemotherapy in Melitensis Infection.**]—*Riforma Med.* 1927. Jan. 31. Vol. 43. No. 5. pp. 100–101. [8 refs.]

The authors carried out series of experiments to test the bactericidal action of gonacrine and tripaflavine of the acridine group on *M. melitensis* in vitro. The power of each was about the same. In a dilution of 1 in 125,000 they inhibited growth in a broth culture. It was next found that the addition of normal human serum, in a proportion of one part to four of culture, raised the inhibiting power to more than double ; in fact, no growth occurred with a dilution of 1 : 256,000, but there was growth with 1 : 512,000. It may be inferred that the exaltation would be still greater if immune serum were used in place of normal serum.

Irradiation of the solution for 25 minutes has no effect on its potency. Addition of chrome alum leaves the bactericidal power of the acridine compounds unchanged, but potash alum reduces it to some extent.

H. Harold Scott.

BURNET (Et.). Agglutination croisée du *Bact. tularence* et des *Brucella* dans la tularémie et la fièvre méditerranéenne. [**Cross Agglutination of *Bact. tularense* and *Brucella* in Tularaemia and Undulant Fever.**]—*Arch. Inst. Pasteur de Tunis.* 1927. Apr. Vol. 16. No. 1. pp. 90–91.

The author refers to the work of FRANCIS & EVANS who came to the conclusion that it was advisable, on account of cross agglutination, to test a serum sent to the laboratory for diagnosis of tularaemia for undulant fever also. He takes up the other side of the same subject for sera requiring confirmation in respect of the diagnosis undulant fever. His results were: (1) 12 sera of undulant fever cases, giving with the corresponding organism agglutinations of 1–400 to 1,000, gave no agglutination with *B. tularense* even at 1–20; (2) 3 sera of guinea-pigs inoculated with *Brucella melitensis*, which agglutinated *melitensis* and *abortus* at 1–1,200, did not agglutinate *B. tularense* at 1–20; (3) 7 typhoid fever sera and 2 of epidemic typhus did not agglutinate *B. tularense* even at 1–20. He concludes that, although the serum of patients suffering from tularaemia is often agglutinating for *Br. melitensis* and *Br. abortus*, this must be non-specific: it is not the case that the sera of patients suffering from undulant fever agglutinate *B. tularense*. Attention must be paid, however, to the very unequal sensitiveness of strains of Brucella to agglutination and particularly to the type *paramelitensis*, which is agglutinated by normal sera and even spontaneously.

W. F. Harvey.

ANDREI (Giuseppe). Sul valore di alcuno metodi proposti per la differenziazione del "B. melitensis" dal "B. abortus."—*Pathologica.* 1927. Mar. 15. Vol. 19. No. 425. pp. 119–121.

ZANOTTI (Ugo). Un caso di "febbre di Malta" in provincia di Brescia.—*Giorn. di Clin. Med.* Parma. 1926. Dec. 31. Vol. 7. No. 18. pp. 748–751.

OROYA FEVER AND VERRUGA PERUANA.

Noguchi (Hideyo). **Etiology of Oroya Fever. VI. Pathological Changes observed in Animals Experimentally infected with *Bartonella bacilliformis*. The Distribution of the Parasites in the Tissues. VII. The Response of the Skin of *Macacus rhesus* and Anthropoid Apes to Inoculation with *Bartonella bacilliformis*.**—*Jl. Experim. Med.* 1927. Mar. 1. Vol. 45. No. 3. pp. 437–454. With 27 figs. on 4 plates. [11 refs.]; 455–463. [8 refs.]

vi. "The pathological changes observed in the organs in *Macacus rhesus* monkeys which have succumbed to severe infection with *Bartonella bacilliformis* are similar to those found in human organs in persons dying of Oroya fever.

"The characterisitc changes in the liver are the zonal necrosis of the cells around the hepatic veins, involving active macrophagocytosis of invading polymorphonuclear leucocytes in the necrotic areas, and a marked endothelial hyperplasia in the sinusoids or around the portal veins. In some instances there is fatty infiltration of hepatic cells.

"In the spleen persistent hyperplasia of the endothelial cells of the capillaries leads to the formation of minute foci of infarction, owing to occlusion of the lumina. The follicles are dispersed or reduced, and there is an active macrophagocytosis of cellular débris, polymorphonuclear leucocytes, and erythrocytes. In some specimens an increase in normoblasts is noted. Pigment is sometimes present.

"The lymphatic system shows general progressive endothelial hyperplasia, with active invasion of macrophages which contain polymorphonuclear leucocytes, erythrocytes, and greenish or dark pigments.

"In the bone marrow there is increased activity of macrophagocytes. Numerous normoblasts are found in some instances.

"*In one monkey, sacrificed during the course of infection, small, verruga-like nodules were found in the lungs and spleen.*

"*Bartonella bacilliformis* has been detected miscroscopically, though in small numbers, in all tissues showing histological changes. Parallel cultural determinations of the presence of *Bartonella bacilliformis* in the blood, liver, spleen, lymphatic glands, bone marrow, and local lesions established the relationship between the pathological conditions and the presence of the parasite. The organism seems to persist longest in the lymphatic glands. Cultural methods offer a simple and conclusive means for the determination of the presence or absence of the infecting organism."

vii. This report deals with verruga-like lesions from infection with cultures and growths of *Bartonella bacilliformis*. It is a curious fact that from the lesions of animals experimentally infected, which are generally very chronic, there are rarely any secondary nodules, though the skin around the lesion must frequently be more or less bathed in blood and serum containing the infective organisms. The author asks, why is this? and he endeavours to find out. He shows that the organism does not pass through the intact skin though it infects easily when the skin is scarified or the organism is given intradermally. An ordinary local irritation in an infected animal will not give rise to a verruga nodule at that place; thus they are not due to mechanical factors.

He divides the infection into four stages—Incubation; Initial stage, which is a condition of pure angio-endothelioma; Mature stage, when there is also connective tissue proliferation and occasional penetration of the epidermis into the tissue with evidence of the infecting organism in both stages; lastly a stage of Retrogression.

P. W. Bassett-Smith.

NOGUCHI (Hideyo). **Etiology of Oroya Fever. VIII. Experiments on Cross-Immunity between Oroya Fever and Verruga Peruana.**— *Jl. Experim. Med.* 1927. May 1. Vol. 45. No. 5. pp. 781–786. [6 refs.]

"Nine monkeys (*Macacus rhesus*) and a chimpanzee which had recently recovered from an infection with the Oroya strain of *Bartonella bacilliformis* were tested for immunity against the verruga strain of *Bartonella bacilliformis* as well as against the homologous strain. Complete immunity to both strains was demonstrated. The result establishes the identity of the strains and is in agreement with the result of comparative serological study.

"The criteria of recovery include not only the subsidence of febrile reactions and local lesions but also a negative result of cultural tests of blood and lymphatic gland tissue.

"Recovery may occur as early as 1 month after inoculation, but in most instances a period of 2 to 5 months is required for the completion of convalescence."

P. W. B-S.

NOGUCHI (Hideyo). **The Etiology of Verruga Peruana.**— *Jl. Experim. Med.* 1927. Jan. 1. Vol. 45. No. 1. pp. 175–189. With 5 charts in text & 3 plates (1 coloured). [6 refs.]

The author first notes the similarity of the epidemiology and some of the clinical symptoms of verruga and Oroya fever, though the former is chronic and the latter acute. Verruga can be directly transmitted, but proof is lacking for Oroya fever. Young rhesus monkeys can be infected with *Bartonella bacilliformis* with the production of signs and symptoms of both diseases.

"A saline suspension of a subcutaneous nodule excised from a verruga patient, and kept in the refrigerator for 14 days, on inoculation into two young *Macacus rhesus* monkeys (Nos. 33 and 34) induced irregular febrile reactions and enlargement of the lymph glands, and in one instance a subcutaneous nodule arose, independently of direct inoculation, on the tail. A microorganism has been isolated from the blood of both animals, and from the experimental nodule, which in pathogenic properties and in cultural and morphological characteristics is indistinguishable from the strain of *Bartonella bacilliformis* isolated from a case of Oroya fever.

"The spontaneous skin lesion of Monkey 34 and the subcutaneous nodules induced by intradermal inoculation of cultures of the microorganism were histologically typical of experimental verruga lesions in monkeys and identical with the skin lesions induced in monkeys by *Bartonella bacilliformis*. The organism, like *Bartonella bacilliformis*, is an intracellular parasite, being found in the cytoplasm of the proliferating endothelial cells of the lesions and in the erythrocytes of the blood.

"The same variations in the manifestations of disease which have been noted in experimental infection with *Bartonella bacilliformis* were observed in the experimental verruga infection. In the second passage (Monkey 41) the infection induced by local inoculation of cultures was severe both locally and constitutionally and was accompanied by marked anemia. The organisms were found in the red cells in large numbers. In the third passage the systemic infection was less severe, but the local lesions were more striking.

"Detection of the parasites in the blood is far more certain by the cultural method than by microscopic examination, the latter procedure being successful only in rather severe infections. The result of blood culture is therefore the decisive method in the final diagnosis of the disease.

"Preliminary serological study shows that the organism isolated in the present instance from the skin lesion of a verruga patient and that previously obtained from the blood of a case of Oroya fever belong to the same serological group.

"The data obtained justify the conclusion that verruga peruana is caused by *Bartonella bacilliformis*. They also definitely establish the fact that the inoculation of blood or sanguineous exudate from lesions of verruga peruana is capable of inducing in susceptible individuals a severe febrile systemic infection, such as that to which Carrion succumbed. The designation 'Carrion's disease' is therefore the appropriate one for both forms of the infection.

"*Bartonella bacilliformis* may be regarded as a bacterium, since it has the essential features of that group of micro-organisms."

P. W. B-S.

Hercelles (Oswaldo). Acerca de la "Fiebre Grave de Carrión." [**On Carrion's Disease.**]—*An. Facul. de Med.* Lima. 1926. Vol. 9. Nos. 1, 2 & 3. pp. 94–96.

The author states that he has cultivated in blood-agar with rabbit's testicle the organism of Oroya fever. This can be seen after 24 hours in the form of small bodies with a rotatory movement by the dark-ground illumination, and as small cocci, or encapsulated diplococci, after three days. He mentions in a parenthesis that he treated a patient with a vaccine made from this "with surprising results." [No details are given.]

H. Harold Scott.

JAPANESE RIVER FEVER.

Hayashi (Naosuke), Oshima (Fukuzo), Eguchi (Sueo) & Hozumi (Kanichi). **On Tsutsugamushi Disease and its Virus.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 2. pp. 925–929. With 7 figs. (2 coloured) on 3 plates.

In the Niigata Prefecture, Japan, the Shinano river region is the most infectious area. The case mortality is 40 per cent. Animal experiments with Japanese monkeys, guineapigs and rats were made; in the former the course was like that in man. Twenty years ago Hayashi described the Rickettisa-like bodies as the etiological agents.

For protection the use of a proper dress and excision of bite area are recommended. An immune serum may be prepared by passage of the virus through birds, which reduces its virulence. This has been tried on eight children with advantage.

P. W. Bassett-Smith.

Nagayo (Mataro). **On the Virus of Tsutsugamushi Disease.**—*Far Eastern Assoc. Trop. Med. Trans Sixth Biennial Congress, Tokyo, 1925.* Vol. 2. pp. 937–939.

In 1923 intradermal was found to be more efficacious than subcutaneous inoculation of the virus. A monkey (*Macacus fuscatus*) was infected with 3 strains. The skin, lymph glands, spleen and blood were examined. When skin was stained with Azur 2, cells containing round,

single, diplococcoid or bacillary bodies stained blue were seen in the corium and were also sometimes found free or in polymorphs. These bodies increase in number with the length of infection. Adjacent lymph glands show proliferation and detachment of the endothelial cells, haemorrhages and necrosis. The condition in the spleen is similar. The author found these bodies also in the mite, especially in the ovum. The virus is non-filterable, non-cultivable, transmitted only by certain mites and is difficult to stain. It is more probably bacterial than protozoal.

P. W. B-S.

TROPICAL AND ENDEMIC TYPHUS.

Norris (V. H.). **A Case of Tropical Typhus Fever in Singapore.**—*Malayan Med. Jl.* 1927. Mar. Vol. 2. No. 1. pp. 44–45.

The author describes the case of a rather prolonged fever in a European which commenced gradually and fell by lysis. It was at first mistaken for enteric, but the laboratory findings disproved this and the Weil-Felix reaction, at a titre of 1 in 400, was suggestive of typhus. During convalescence there was some peripheral neuritis and oedema. Recovery was complete. The intense prostration with loss of knee jerks was considered to clench the diagnosis.

P. W. Bassett-Smith.

Bablet (J.), Mesnard & Polidori. Premiers résultats d'une enquête sur le typhus exanthématique au Tonkin. [**Typhus in Tonkin.**] —*Bull. Soc. Path. Exot.* 1926. Nov. 10. Vol. 19. No. 9. pp. 765–770. [3 refs.]

Yersin & Vassal in 1908 reported the presence of typhus in South Annam. Since that time only two records of cases can be found, one at Saigon and one in Hanoi. The authors now describe an epidemic in the prison of Hanoi in 1926, 150 cases with 16 deaths. It is pointed out that the foundation of the Pasteur Institute of Hanoi enables the necessary laboratory researches to be carried out for the establishment of the diagnosis, which is often difficult, since in the dark skinned natives the rash is very hard to detect.

P. W. B-S.

Maxcy (Kenneth F.). **An Epidemiological Study of Endemic Typhus (Brill's Disease) in the Southeastern United States, with Special Reference to its Mode of Transmission.**—*Public Health Rep.* 1926. Dec. 24. Vol. 41. No. 52. pp. 2967–2995. With 1 text fig. & 4 maps. [29 refs.]

In 1910 Brill drew attention to a typhus-like disease of low infectivity and mortality which occurred in the U.S.; this he thought was a new clinical entity. In 1912 Anderson & Goldberger found that as in Mexican typhus (Tarbadillo) Rhesus monkeys could be infected by inoculation which rendered them immune to both diseases. They therefore, concluded that Brill's disease was identical with typhus. Some cases could be traced to imported typhus, but many were definitely endemic and sporadic: these, though like Brill's disease,

gave a positive Weil-Felix reaction. The present report refers to cases from Alabama and Savannah, Georgia, where imported cases are nil or rare. They include 104 from the former and 93 from the latter, which form a definite clinical group not distinguishable from typhus, though of the Brill type, and thus called endemic typhus.

The epidemiological characters are described, with the seasonal and local distribution. The occupations distinctly suggest that those engaged in trades especially connected with food show an increased risk of infection, but the infection was *not associated with lice.* It was assumed, therefore, that a reservoir exists other than man, and that this reservoir is in rodents from which the disease is occasionally transmitted to man.

P. W. B-S.

DENGUE AND UNCLASSED FEVERS.

Dive (G. H.). **Dengue in Aden : a Clinical and Statistical Survey, with an Appendix on Fevers in Aden.**— *Jl. Roy. Army Med. Corps.* 1927. Apr. Vol. 48. No. 4. pp. 241–247.

The author has analysed 100 consecutive cases of dengue-like fevers among the troops at Aden, and places them into two groups. (1.) Typical dengue (showing stages of initial fever, remission and terminal fever), 41 cases. (2.) Terminal (not showing these stages), 59 cases divided into ; (*a*) a short fever simulating 3 day fever ; (*b*) a low continued fever ending in crisis ; (*c*) a longer or 5 day fever, ending in lysis ; (*d*) cases suggesting a short paratyphoid fever. In none were spirochetes found in the urine, but clinical and epidemiological factors, including the vector, *Aedes argenteus*, make the diagnosis of dengue definite in Aden. This fever occurs generally between April and July, and for fresh non-immunes again in September, when mosquitoes are abundant. The author is doubtful whether sandfly fever ever exists in Aden. He notices a low continued fever invariably associated with polyneuritis which in Aden appears to be a manifestation of beriberi. Enteric and malaria are rare.

P. W. Bassett-Smith.

Richardson (Shaler). **Keratitis as a Complication of Dengue Fever.**— *Southern Med. Jl.* 1927. Jan. Vol. 20. No. 1. pp. 32–36. [73 refs.]

Eye complications in dengue are infrequent and rarely recorded, but the author has seen six cases of keratitis in the first week of convalescence. Two are described in detail. No infecting organisms were found by culture. Herpes of the lids was present in some ; the fundus was always normal. It is suggested that the disease is due to a toxic Gasserian ganglionitis. The condition is undoubtedly very rare, since the author states that in the epidemic at Jacksonville he saw only 6 cases of keratitis among 20,000 cases of dengue. Further study whether the infectiousness of the herpetic vesicles is a cause of the trouble is required.

P. W. B-S.

McCallum (F.) & Dwyer (J. P.). **Dengue as a Cause of Death.**—*Med. Jl. Australia.* 1927. Jan. 1. 14th Year. Vol. 1. No. 1 pp. 10–15. [10 refs.]

From a careful study of the statistics in Queensland the author shows that though the mortality of dengue is almost negligible (0·3 per cent.), yet it is not nil, and "in recurrent epidemics there is a tendency to increased severity and fatal cases become more frequent" (Hare). It is necessary that more care in certification should be taken as also in the diagnosis.

P. W. B-S.

Suldey (E. W.). La dengue du Soudan. [**"Dengue" in the Sudan.**]—*Bull. Soc. Path. Exot.* 1926. Dec. 8. Vol. 19. No. 10. pp. 881–884. [2 refs.]

In the author's experience, Soudanese "dengue" may vary in duration from 3 to 8 days, the severity being generally slight. Some cases are of an ambulant type, others attended by considerable fever and marked pains; neither fever nor exanthem are constant signs. He observed a "lethargic" form in a European not before described. He states that the epidemic at Bamako did not cause any deaths, there were no severe complications and relapses were rare. In the differential diagnosis, yellow fever was the most important disease; the detection of albuminuria was significant. It is noted that *Phlebotomus duboisqui* and *P. minutus* were commonly found. It was not possible to state definitely whether the disease was a form of phlebotomus fever or dengue, but he thinks that sand flies were the carriers rather than stegomyia, the prevalence of which did not coincide so well with the incidence of the cases.

P. W. B-S.

Perves. Epidémie de "dengue" à la marine de Dakar. [**Epidemic of "Dengue" in the Naval Forces at Dakar.** *Bull. Soc. Path. Exot.* 1927. Jan. 12. Vol. 20. No. 1. pp. 92–99. [5 refs.]

The author states that there was a small epidemic of dengue in a ship at Dakar in 1913. The epidemic now reported occurred between August and October 1926. There were 105 cases among 525 people, with 2 deaths. Men, women, and children were affected. The patients were but a short time in the hospital, and the symptoms were not exceptionally severe, the prognosis being generally good, except for the very old and those greatly debilitated by diseases of the liver and kidney, among whom there were deaths. Stegomyia were abundant as well as other mosquitoes; their destruction was the best prophylactic measure. Blood examinations gave no information.

P. W. B-S.

Lépine (Pierre). Contribution clinique et expérimentale à l'étude de la fièvre de trois jours en Syrie. [**Three Day Fever in Syria: Clinical and Experimental.**]—*Bull. Soc. Path. Exot.* 1927. Mar. 9. Vol. 20. No. 3. pp. 251–260. With 1 text fig. [10 refs.]

The research was carried out at the University of Beyrout. Great care was taken to include only typical forms of three day fever, of which there were 127. The ages of greatest incidence were 19 to 35.

The author states that the virus is present on the first day of fever, that it is in the plasma and is not endoglobular, but BIRT'S filterable virus view was not confirmed. The incubation was short—three days and eight hours. The virus was destroyed at 55° C. in 10 minutes; no visible germs were ever found in the blood and no culture was obtained.

The experiments were inconclusive, and will be continued.

P. W. B-S.

YAKIMOFF (W. L.). Un cas de fièvre à cinq jours à Petrograde. [**Five Day Fever in Petrograd.** *Ann. Soc. Belge de Méd. Trop.* 1926. Dec. Vol. 6. No. 3. pp. 275–280.

The author describes a case of five day fever in a man aged 24. He had been in Odessa, but arrived at Petrograd in 1922. The symptoms were at first like those of malaria, but with peculiar intervals of five days and high spikes (6) associated with pains in the bones. Lice were caught on his body one month before arrival at Petrograd. Spirochaetes were demonstrated from the blood on one occasion only, but did not appear to be *Sp. obermeirii*. Repeated injections of neosalvarsan were curative.

P. W. B–S.

PINOT (R.). Note sur une épidémie de fièvre de sept jours observée sur les navires de guerre stationnés à Saigon (mai-juillet 1926). [**Seven Day Fever on War Ships at Saigon.**] —*Arch. Méd. et Pharm. Nav.* 1926. Oct.–Nov.–Dec. Vol. 116. No. 4. pp. 305–321. [16 refs.]

The author describes a small epidemic of a short fever affecting both those in the ships and the marines on shore, which was apparently carried by stegomyia (*Aedes argenteus*). In none of the cases were spirochetes demonstrated in the blood.

P. W. B-S.

KALA AZAR.

RAMAN (T. K.). **Kala-Azar in Madras.**—*Madras Med. College Mag.* 1927. Mar. Vol. 6. No. 4. pp. 273–294. With 3 graphs & 6 figs. on 3 plates. [11 refs.]

The paper gives the results of the analysis of 406 cases of kala azar admitted to the General Hospital, Madras, during 1924 and 1925 and certain facts which have come to light regarding the bionomics of *Phlebotomus argentipes* in that city. The racial incidence of the 406 cases gave Europeans 2, Chinese 1, Indians 339, Anglo-Indians 64. The cases varied in age from 3 to 62, the majority being between 10 and 30. The hospital patients showed a preponderance of males, but such preponderance is not borne out by the experience of private practitioners. Of the 406 cases only 115 gave a definite history of onset, which in the majority of these occurred in January, February and March. The distribution of the cases in the city showed that, as stated by KORKE in 1912 (this *Bulletin*, Vol. 2, p. 432) George Town was the cradle of the disease. Of 288 cases 128 came from this part of the city, while 71 were from Vepery, including New Town, and 20 from Triplicane and Mylapore, 16 from Royapuram and 15 from Chintadripet. Outside the city but within Madras Presidency cases came from Kavalpatnam, Tinnevelly Bridge, Dhanushkodi and Calicut. Cases were treated with sodium antimony tartrate or urea stibamine. Of the 406 cases 186 were cured. Of the remaining 220, 50 were known to have died, others went away without treatment or with incomplete treatment. In 4 cases during the course of the treatment herpes developed over the course of one or other of the dorsal nerves. In one case leishmania were found in the liquid from the vesicles.

Under the heading sand flies, information is given regarding the life history of these insects. They could be caught in large numbers during July, August and September. During December and January very few or none could be found, while they were again on the increase during April and up to the hottest season of the year (May to June), when none could be captured. Thus in Madras they are at a minimum during the hottest and coldest seasons of the year.

C. M. Wenyon.

ADAMOPOULOS (Charalambos). Le kala-azar dans le département de Messénie. **Kala Azar in Messenia, Greece.**—*Grèce Méd.* 1926. July–Aug. Vol. 28. No. 7–8. p. 26.

From information collected it is evident that kala azar has existed in the department of Messenia at the S. West corner of Greece for many years. It has been known under the name Benokladi and occurs especially in the districts at the base of mountains. Since 1914 the author and Dr. ALIFERIS have diagnosed microscopically about 500 cases of the disease. Apart from these the author himself has diagnosed more than 100 cases, while other physicians have identified others. In all from 750 to 800 cases have been microscopically diagnosed in the department during the past ten years. The majority are in children who are at most four years of age. It is of interest to note that during the last five years the area of most intense infection appears

to have changed from one district to another. In treatment intravenous injections of tartar emetic, stibyl or stibyal have given very satisfactory results.

C. M. W

Artamonoff (A. S.). Zur Frage der Verbreitung der innerlichen Leishmaniasis in Samarkand und die Heilung der Krankheit durch die Präparate des Stibiums. [**The Distribution of Kala Azar in Samarkand and its Cure by Antimony Preparations.**] —*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Jan. Vol. 31. No. 1. pp. 32–37.

From January 1924 to March 1926 there were registered in the town of Samarkand 138 cases of kala azar of which 71 were Russians. In the old town, with a population of about 65,000, there were 34 cases, while in the Russian quarter, with a population of about 20,000, there were 66 cases. Of the 138 cases 100 occurred in children up to 4 years of age, 26 in those between 5 and 11 years, and the remaining 12 in persons between 12 and 32 years. Of a series of 68 treated cases only 28 recovered, but this bad result was due largely to the fact that the treatment was not continued over a sufficiently long period. There was a definite relationship between the duration of treatment and recovery. Thus, of 9 cases treated for 7 to 10 weeks 5 recovered, while of 21 treated for 6 to 12 months 18 were cured. Various antimony-containing drugs were used but antimony given intravenously was found to be the best.

C. M. W.

Hodgson (E. C.). **Clinical and Pathological Notes on Cases of Kala-Azar.** —*Proc. Assam Branch Brit. Med. Assoc. Annual Meeting, Silchar, 1st and 2nd March, 1926.* pp. 11–16.

The author discusses certain difficulties encountered in the clinical diagnosis of kala azar in Assam. The main features of the disease are splenomegaly, hepatic enlargement, anaemia, pyrexia and leucopenia while the blood gives the aldehyde reaction. With regard to the first four symptoms cases have been seen in which every one of these was absent over fairly long periods, such as a month. The most constant symptom, unless some complicating disease occurs, is leucopenia, the next being anaemia. In these cases one other feature is very constantly present, and that is an increase in the pulse rate to 90 or 110, even when the temperature is normal or subnormal, the rate scarcely rising when the temperature mounts to 102° or 103° F. A failure to recognize this may account for the fact that so many cases, especially those in Europeans, have been treated for enteric fever. More common are the cases showing enlargement of liver and spleen with a normal temperature. These patients as a rule have a history of treatment for malaria or enteric, but usually without disappearance of the enlargement of the spleen and without slowing of the pulse to normal even weeks after the supposed cure. Such are not necessarily errors of diagnosis, for several examples of kala azar with associated malaria infection have been seen and after quinine treatment the temperature has become normal and the general condition improved. Similarly a case of associated enteric fever improved considerably, showed decrease in the volume of the spleen and appeared to be convalescing satisfactorily after having gone through an ordinary attack of enteric fever. The only suspicious signs

were a persistent rapid pulse and a leucopenia. So many of the cases of kala azar admitted to the Shillong hospital have some secondary infection that one is led to wonder whether a preliminary breakdown of resistance may not be a necessary antecedent to kala azar.

The commonest diseases complicating kala azar are gingivitis and pyorrhoea, malaria during the fever season, hookworm and worm infections generally, dysenteries, both amoebic and bacillary, jaundice, oedema, resulting from renal insufficiency, and pneumonia. It comes about, therefore, that in Assam, after making a diagnosis of any disease in an Indian, one must always remember that kala azar may be present also. The successful treatment of these diseases is often followed by such definite improvement that the presence of the underlying malady is unsuspected.

Of a considerable number of drugs experimented with three are mentioned—urea stibamine of Bramachari has been a valuable improvement on tartar emetic, but too much has been ascribed to it; Von Heyden 471 (stibosan) was found to act quite as effectively as urea stibamine, while patients showing toxic symptoms with urea stibamine would not necessarily show them with stibosan. Stibamine glucoside (neostam) of Burroughs and Wellcome was quite as effective, if not more so, than the two other drugs in the 23 cases in which it was tried. A decoction of *Vitex peduncularis*, a reputed cure for kala azar, was found to be useless while scale preparations of antimony were not as effective as sodium antimony tartrate.

Three cases are quoted to illustrate definite resistance to antimony treatment. It is pointed out that this resistance is often the outcome of an incomplete initial treatment. Another point emphasized is the increase in the size of the liver which frequently occurs as a result of the use of the newer organic preparations of antimony. Recession takes place when the antimony treatment is stopped. In certain cases no diminution in the size of the spleen occurs even after complete disappearance of parasites. These cases are extremely resistant to any form of treatment, though recently X-ray appears to be giving gratifying results.

In fatal cases of kala azar ascites is present in most, the heart is usually found dilated and flabby with degeneration of the muscle fibres, the pancreas is much enlarged, hard and fibrotic, the mesenteric glands are enlarged in cases dying with chronic diarrhoea, while the kidneys show an acute inflammation and desquamation of the tubule epithelium which leaves a suspicion of antimony poisoning.

C. M. W.

Vasile (B.). Contributo alla conoscenza dell' infezione associata kala-azar-malaria. [**Association of Kala Azar with Malaria.**]—*Pediatria.* 1927. Apr. 1. Vol. 35. No. 7. pp. 376–380. [8 refs.]

Examination of the literature has shown that the association of kala azar with other infections is a comparatively rare condition, only a few cases of concurrent undulant fever and malaria having been recorded. From the histories of 1,132 cases of kala azar seen at the Catania clinic during 1910 to 1925 Paradiso could obtain evidence of malaria in only one. He further observed that in the intense malaria foci cases of kala azar are very rare, while they are encountered with some frequency

in non-malarious localities. The author of the present paper, writing from Palermo, describes in detail a case of kala azar in a child 21 months old who suffered at the same time from malaria.

C. M. W.

Low (George C.) & Sayers (Edward G.). **The Early Diagnosis of Kala-Azar.**—*Jl. Trop. Med. & Hyg.* 1927. Feb. 15. Vol. 30. No. 4. pp. 46–48. With 1 chart in text.

The difficulty which may occur in the early diagnosis of kala azar is illustrated by the case of an Indian who was admitted to hospital for pneumonia. The patient had not been ill before and though all the tests applied threw no light on the situation it was thought he might be suffering from influenza, though the spleen was enlarged and hard but not tender. The liver also was slightly enlarged. It was then concluded that the illness was due to an atypical form of paratyphoid and suitable diet was instituted. The temperature remained remitting and irregular for 4 weeks. After this a more generous diet was given and the temperature fell to normal, while the general condition improved. Convalescence was uneventful, the temperature remaining normal for 4 weeks, the patient gaining a stone in weight. As the spleen remained in its former condition it was decided to puncture it before permitting the patient to rejoin his ship. The result was that abundant leishmania were discovered and a diagnosis of kala azar established.

C. M. W.

Low (George C.) & Cooke (W. E.). **A Congenital Case of Kala-Azar.**—*Lancet.* 1926. Dec. 11. pp. 1209–1211. With 3 text figs.

An Englishwoman aged 33 was incompletely treated with urea stibamine for what was thought to be kala azar in Calcutta, after which she returned to England, where she again became seriously ill and was given further injections of the same drug, as a result of which improvement occurred. About 2½ months later a healthy child of normal weight was born. It was not nursed at any time by the mother, who after her confinement began to fail in health again and was admitted to the Hospital for Tropical Diseases, where it was found that she showed all the symptoms of kala azar. As there was no doubt as to the diagnosis treatment with Von Heyden 471 (stibosan) was commenced. After the administration of 4 gm. of the drug she was discharged to all intents and purposes cured.

For the first fortnight after its birth the child progressed normally. It then had a convulsion, was not well for a week and did not completely recover. About 7 weeks later it had bad diarrhoea and pain and was taken into a nursing home. During her period in hospital the mother inquired if it were possible that the child's illness could be kala azar and examination of the child was suggested, and this was done about a month after the mother was discharged. The child did not look well, but as it had no splenic enlargement no puncture was made. During the next 6 months the child was not well, while the abdomen became prominent. It was then brought again for examination. There was marked anaemia, emaciation and protuberant abdomen due to an enormously enlarged spleen. There was high temperature of a remitting type, while the blood count showed R.B.C., 1,600,000; W.B.C., 2,600; Hb. 30 per cent.; poikilocytosis and nucleated red

cells were present. A spleen puncture revealed the presence of leishmania. The child was treated with stibosan intramuscularly and made what appeared to be an uninterrupted recovery. About 3 months after the diagnosis of kala azar had been established in the child the mother again became ill. Spleen puncture was then performed and the presence of leishmania confirmed the original diagnosis.

The interesting point about the child is that of a congenital infection. Owing to the mother's illness the child was not nursed by her and was mainly looked after by other people. It does not seem probable that infection took place through contact or orally so that the most reasonable conclusion is that infection took place *in utero*. Against this might be urged that when seen at the age of 7 months there was no enlargement of the spleen and that the illnesses from which the child had suffered were those common in infancy. It was only 6 months later that marked enlargement of the spleen was noted and the diagnosis of kala azar made. It is evident that the increase in size of the spleen took place after the 7th month. The authors are probably correct in their interpretation of the case, but for a final conclusion it would be necessary to find leishmania immediately or soon after birth.

C. M. W.

Bhaduri (B. N.). **A Case of Opacities of the Lens occurring as a Sequel to an Attack of Kala-Azar.** *Indian Med. Gaz.* 1927. Mar. Vol. 62. No. 3. p. 144. With 1 diagram in text.

Two months after undergoing a course of treatment for kala azar a young man 22 years of age began to suffer from defect of vision. Examination revealed the fact that there was some opacity of the lenses. It seems possible that the condition was brought about by kala azar. With the improvement in the patient's health further impairment of vision ceased, and when examined a year and a half later he was found to be in the same condition.

C. M. W.

Graziano (Francesco). Nuovo contributo alla terapia del Kala-Azar. [**Treatment of Kala Azar.**] —*Pediatria.* 1927. Apr. 1. Vol. 35. No. 7. pp. 359–364. [62 refs.]

During the ten years 1915 to 1925 116 cases of infantile kala azar came to the notice of the Clinic in Palermo. Of these eight remained in hospital and were successfully treated with tartar emetic, the quantity of drug given to each child varying from 80 to 118 centigrams. The remaining patients either did not enter the hospital or left it shortly after treatment was commenced. Some continued to come for treatment as out-patients, others discontinued treatment or did not even begin it. Of the 108 patients 71 died, 17 recovered and 20 were not traced. Of the recoveries 11 had discontinued treatment, 3 had employed inunctions for periods of two months to two years, 1 was still under treatment and 2 had had no treatment. In view of these figures it is evident that proper treatment with tartar emetic, as claimed by the numerous authors quoted in the paper, will effect a cure in a large percentage of cases. Furthermore it is clear that spontaneous recovery can take place in a small percentage of cases.

C. M. W.

Struthers (Ernest B.). **"Neostam," Stibamine Glucoside, in the Treatment of Kala Azar. (A Preliminary Report.)**—*China Med. Jl.* 1927. Jan. Vol. 41. No. 1. pp. 21–28.

The paper describes the treatment of 18 cases of kala azar with Burroughs Wellcome & Co's neostam (stibamine glucoside, the nitrogen glucoside of sodium p-aminophenyl stibinate). It has a toxicity of about 1/20 of sodium antimonyl tartrate and is used intravenously in a 2 per cent. solution. It is a colourless powder fairly readily soluble in distilled water. Injections are given on alternate days beginning for an adult of 100 lb. weight with a dose of 0·05 gm. and increasing by 0·05 gm. till a maximum of 0·2 gm. is reached. This is continued till the patient has had a total of 2 or 3 gm. A rise in temperature, nausea or headache indicate that the last dose has been too large, in which case the next dose should be reduced by 0·05 or 0·03 gm. The total number of doses required is from 12 to 15 during the course of a month or 5 weeks. Of the 18 patients thus treated 3 died, one a boy of 14, in a hopeless condition when admitted, one a child of 12 with cancrum oris, and one an adult of 36 who developed bronchopneumonia. All the others were cured, with the exception of one in which the result is still in doubt. It is concluded that neostam is much superior to sodium antimony tartrate or tartar emetic for the treatment of kala azar.

C. M. W.

Korchitz (E. V.). [**On the Treatment of Infantile Leishmaniasis with Stibenyl.**]—*Pensée Médicale d' Uzbekistane.* Tashkent. 1926. Vol. I. (V.). No. 1. pp. 36–37. [In Russian.]

The author describes an advanced case of kala azar [erroneously referred to as " Orientbeule " in the German summary] in a seven year old boy. Though the patient was in extremis, a definite improvement was observed after seven injections of stibenyl, administered every other day (dose 0·1 gm.). After the thirtieth injection, the patient's health was fully restored. The author strongly recommends stibenyl and quotes the following words of Professor Smorodintsev (*Kazan Med. Journ.*, 1926) in support of it : " This preparation sterilizes the organism within ten days in 73 per cent. of cases of kala azar. It should be considered as the best antimony derivative known, both on account of its slight toxicity and the rapidity with which most of it is excreted."

C. A. Hoare.

Sanyal (Charu Chandra.) **Rectal Administration of Antimony for the Treatment of Kala-Azar.** —*Calcutta Med. Jl.* 1927. Feb. Vol. 21. No. 8. pp. 405–408.

The author describes the treatment of 4 cases of kala azar in children by the rectal injection of solution of stiburia (The Union Drug Co. brand of urea stibamine). Response to the treatment was in all 4 cases rapid. Unfortunately the only indication of the dosage used is the statement that in one of the cases treatment was commenced with a dose of 0·05 grams dissolved in 5 cc. of sterile or ordinary pure water. Though the author admits that the cases are published prematurely he feels justified in drawing attention to the method of treatment owing to the difficulty of treating children by intravenous injections.

C. M. W.

Auricchio (Luigi). Considerazioni e ricerche sulla terapia della leishmaniosi infantile. [**Treatment of Infantile Leishmaniasis.**]—*Pediatria.* 1927. Mar. 15. Vol. 35. No. 6. pp. 289–300. [8 refs.]

Four cases of kala azar were treated at the clinic in Naples with "eparseno" (aminoarsenophenol). As the drug did not control the disease in any way intravenous injections of tartar emetic were substituted. The latter drug has given consistently good results as evidenced by the 200 cases reported in the paper. Of those which were not lost sight of 165 were cured and 27 died. The mortality was due to bronchopneumonia in 12 instances, acute enterocolitis in 4 and ulcerative stomatitis in 2. In the majority of cured cases the quantity of tartar emetic administered varied from 0·20 to 0·60 grams given during 1 to 3 months. The advantage of treating cases as out-patients so as to avoid hospitalization is emphasized.

C. M. W.

i. Gupta (B. M. D.). **A Note on the Parasite of "Dermal Leishmanoid".**—*Indian Med. Gaz.* 1927. Jan. Vol. 62. No. 1. pp. 11–12. [3 refs.]

ii. ——. **Further Observations upon "Dermal Leishmanoid".**—*Ibid.* Apr. No. 4. p. 199.

iii. Brahmachari (Upendra Nath) & Dutt (Anant Mohan). **Chemotherapy of Antimonial Compounds in Kala-Azar Infection. Dermal Leishmanoid with Positive Flagellate Culture from the Peripheral Blood. Part III (New Series).**—*Calcutta Med. Jl.* 1927. Feb. Vol. 21. No. 8. pp. 401–404. With 1 coloured plate.

i. The author notes that the condition known as dermal leishmanoid has now become a commonplace at the School of Tropical Medicine in Calcutta. Every month some 3 or 4 cases are seen. In the great majority the patients have been cured of kala azar some months or, more usually, years before the skin eruption in the form of small leucodermic spots appears. In a few instances no history of previous kala azar can be obtained but all the patients come from kala azar areas. Apart from the skin lesions the general health of the patients is good. Films from the lesions show leishmania but blood culture and spleen puncture, when any enlargement of the organ has permitted the operation, are invariably negative. The question arises as to whether the organism is *Leishmania donovani* or *Leishmania tropica*. A culture obtained from a skin lesion was injected into mice. One of the animals killed 94 days after inoculation was found to have an enormously enlarged spleen but though smears from the organ were negative a culture of leishmania was obtained from it. The parasite of the dermal leishmanoid is thus able to cause a systemic infection in mice.

ii. Returning to the subject of dermal leishmanoid the author points out in the first place that in the early stages there may be difficulty in finding leishmania in smears from the non pigmented tiny spots on the skin. If, however, a small fragment of tissue be removed and planted into N.N.N. medium a culture usually results. At later stages, when the granulomatous nodules have developed, discovery of leishmania by direct examination is very much easier. In the second place the author records the case of a Hindu lady about 20 years of age who developed the dermal condition and had been suffering from fever for 8 months. The spleen and liver were not palpable and though the aldehyde reaction

was negative a culture of leishmania was obtained from the vein blood. The author concludes that the patient was suffering from kala azar and the cutaneous infection. All cases of dermal leishmanoid previously seen have been free from kala azar but the occurrence of the two conditions together opens up the question of the relationship of the organisms in the two diseases.

iii. An account of a case of dermal leishmanoid in which the skin eruption first made its appearance while the patient was on a course of urea stibamine for kala azar, of which he was subsequently cured. The skin eruption, however, proved to be very resistant to treatment, though it diminished on the trunk and extremities after a course of bi-weekly intravenous injections of urea stibamine. In most cases of dermal leishmanoid the skin eruption appears some time after the cure of the kala azar condition has taken place. A coloured plate illustrates the patient's condition.

C. M. W.

i Foster (Percy). **A Note on the Control of Kala-Azar Outbreaks by Means of Therapeutic Measures.** *Proc. Assam Branch Brit. Med. Assoc. Annual Meeting, Silchar, 1st and 2nd March, 1926.* pp. 17–18.

ii. Napier (L. Everard) & Foster (Percy). **The Control of Kala-Azar on Tea Estates.**—*Indian Med. Gaz.* 1927. Feb. Vol. 62. No. 2. pp. 76–80. With 2 text figs.

i. With improvement in the treatment and diagnosis of kala azar the question arises, Is it still necessary to evacuate infected lines, as in previous outbreaks, or can reliance be placed on treatment? After considering the question from every point of view with Lt.-Col. Christophers and Major Shortt it was unanimously concluded that one would no longer be justified in advising evacuation and burning of infected houses and could safely rely on early treatment of all detected cases.

ii. The authors discuss the question of the control of kala azar on tea estates, basing their arguments on the experience gained from two tea gardens. It is concluded that by segregation and treatment of actual cases alone the disease will not be stopped but will be controlled. Treatment alone gives a lesser degree of success, while transfer of the lines may be expected to completely cut short the epidemic. The last remedy, unfortunately, takes time, is expensive and is unpopular with the coolies. From the practical point of view the policy to adopt is to treat each case as it arises and keep a careful look out for suspicious cases. If this is done a considerable degree of success can be anticipated. One of the writers (P.F.) adds a note to the paper giving his experience of the adoption of this method on two gardens where during the years 1923–1925, 23 and 16 families became infected. All cases were treated with urea stibamine with the result that only 6 and 2 further cases have occurred on the two gardens.

C. M. W.

Shortt (H. E.), Barraud (P. J.) & Craighead (A. C.). **Transmission Experiments in Indian Kala-Azar with** *Phlebotomus argentipes.*—*Indian Jl. Med. Res.* 1927. Jan. Vol. 14. No. 3. pp. 589–600. [3 refs.]

The paper describes in detail a long series of experiments in which 40 mice and 20 hamsters were subjected to 184 bites from a minimum of

152 *Phlebotomus argentipes* known to be infected with *Leishmania donovani*. In no case did an animal become infected. It is concluded that the intensity of exposure to infection was not sufficient to produce infection in these animals and that the results do not invalidate the conclusion that the sandfly transmits kala azar.

C. M. W.

Shortt (H. E.), Craighead (A. C.), Chand (Khazan) & Swaminath (C. S.). **The 'Resistant Non-Flagellate Torpedo and O Bodies' of Row seen in Old Cultures of *Leishmania donovani* in their Relationship to the Production of Infections.**—*Indian Jl. Med. Res.* 1927. Jan. Vol. 14. No. 3. pp. 567–576. [5 refs.]

In 1922 (this *Bulletin*, Vol. 20, p. 103) Row published a paper in which he described the reversion in the test tube of the flagellate form of leishmania to rounded forms or O bodies which were similar in nature to the leishmania which occur in the tissues of man. It was presumed that they were resistant forms and that infection of animals from cultural forms of leishmania depended on their presence and that it would probably be found that the same held good for any insect capable of transmitting kala azar and oriental sore. An examination of these claims by direct experiment by the authors has shown that the flagellate forms of *Leishmania donovani* alone are capable of producing infection in white mice when inoculated intraperitoneally. One such inoculation is usually sufficient to produce infection. The O bodies are produced in cultures irrespective of the desiccation of the medium as claimed by Row and much earlier (7th or 8th day) than the minimum of three weeks given by Row. The bodies are most abundant in the richest cultures. They may appear in infected sandflies after a second or subsequent feed. All the evidence available is against the probability of the O body playing any part in producing infections. In infected sandflies the forms which accumulate in the most anterior part of the pharynx and buccal cavity are all flagellated and to admit Row's hypothesis would be to make the assumption that these forms are not infective.

C. M. W.

Shortt (H. E.) & Swaminath (C. S.). **The Mode of Formation and Morphology of the O Bodies of Row in Old Cultures of *Leishmania donovani*.**—*Indian Jl. Med. Res.* 1927. Jan. Vol. 14. No. 3. pp. 581–587. With 31 figs. on 1 plate. [9 refs.]

The authors have traced carefully the development of Row's O body in cultures of *Leishmania donovani*. It arises from the short stumpy flagellate forms by a gradual shrinkage and a discarding of the flagellum which breaks off at its point of union with the body. In so doing in the majority of cases it takes with it the intracytoplasmic portion of the axoneme and the parabasal, leaving the nucleus as the only structure in the cytoplasm. By further shrinkage a rounded body measuring 2 microns in diameter is produced. The chromatin mass representing the original nucleus lies near the surface of the body at one point. These O bodies resemble in many respects the minute rounded infective forms which occur in the faeces of certain insects infected with leptomonas such as fleas with *L. ctenocephali*, but in these both the nucleus and kinetoplast are present. The conclusion is

reached that the O bodies are the end-products of degeneration of leishmania and are not viable and that it is unnecessary to assume the existence of resistant forms in the life history of *Leishmania donovani*.

C. M. W.

Shortt (H. E.), Barraud (P. J.) & Craighead (A. C.). **Note on the Infectivity of the Forms of *Leishmania donovani* found in *Phlebotomus argentipes*.**—*Indian Jl. Med. Res.* 1927. Jan. Vol. 14. No. 3. pp. 577–579. [1 ref.]

With a view to determining the infectivity of the flagellate forms of leishmania in *Phlebotomus argentipes* a number of mice were inoculated with the flagellates from the alimentary canal of dissected flies. In all 53 mice were inoculated (18 once, 30 twice and 5 thrice). One of the animals became infected. This was a mouse inoculated on three occasions, on each with the flagellates from a sandfly which had its first feed on a kala azar case, its second on a rabbit and its third on a hamster. In the case of the first fly the interval between its dissection and the feed on the kala azar case was 11 days ; in the case of the second and third the interval was 9 days.

C. M. W.

Napier (L. Everard) & Smith (R. O. A.). **The Development of *Leishmania donovani* in the Gut of the Sandfly *Phlebotomus papatasii*.**—*Indian Jl. Med. Res.* 1927. Jan. Vol. 14. No. 3. pp. 713–716. [5 refs.]

During the kala azar investigations in Calcutta it was found that in the town itself three species of sandfly occurred, viz. *Phlebotomus argentipes*, *P. minutus* and *P. squamipleuris*. Of the last only very small numbers were found while *P. minutus* does not appear to feed readily on man and none of the specimens caught contained human blood. During 1925 the investigation was extended to villages outside Calcutta and here it was found that large numbers of *P. papatasii* occurred in addition to *P. argentipes*. In the hot dry weather the former was found in most of the living rooms in larger numbers than the latter, which, however, was the predominating form in the cattle sheds. A series of preliminary experiments with a view to obtaining development of *Leishmania donovani* in *P. papatasii* have already been described by Napier (1926) in the Annual Report of the Calcutta School of Tropical Medicine for the year 1925. (Report of the Kala-Azar Research Department, p. 21.) It was found that none of 23 *P. papatasii* fed on kala azar cases showed any flagellate infection, though a number of *P. argentipes* fed on the same cases did so. As larger numbers of *P. papatasii* were subsequently caught a larger number of laboratory-bred flies became available so that it was thought advisable to repeat the experiment. In a table the details are set forth. Of 102 *P. argentipes* fed on kala azar cases 43 showed a subsequent flagellate infection while of 101 *P. papatasii* 2 were infected. It is evident that the former is a more suitable host for *L. donovani* and that *P. papatasii*, the distribution of which in India does not correspond with that of kala azar, does not play an important part in the transmission of the disease. It may do so, however, under very favourable conditions.

C. M. W.

Patton (W. S.) & Hindle (Edward). **The Development of Chinese Leishmania in *Phlebotomus Major* var. *Chinensis* and *P. sergenti* var.** —*Proc. Roy. Soc.* 1927. May 2. Vol. 101. Ser. B. No. B 710. pp. 369–390. With 5 text figs. [11 refs.]

The authors give an account of the methods employed by them for collecting, handling, feeding, keeping and dissecting sandflies in connexion with their infection by ingestion of blood from cases of kala azar or infected hamsters. The various receptacles and apparatus are depicted and described. The flies are kept in unglazed earthenware vessels filled with admission tubes and covered with bolting cloth. They are fed from small boxes similar to those usually employed for handling lice and are transferred from one receptacle to another by a specially devised pipette fitted with a plunger which can be so manipulated as to blow a fly from the tube as required.

The feeding experiments gave the following results. Of 102 *Phlebotomus major* var. *chinensis* fed on human kala azar cases 5 showed subsequent development of flagellates. Of 157 flies fed on infected hamsters 122 gave a positive result. Of 202 *Phlebotomus sergenti* var. fed on kala azar patients not one revealed any flagellate infection, while of 1,170 of these flies fed on infected hamsters flagellates were observed in 430. The results of these experiments show that the first-named species is a very favourable host for the development of the leishmania of Chinese kala azar. Furthermore the flagellates which develop in this fly readily extend forwards from the mid gut to the pharynx and buccal cavity, whereas in *P. sergenti* the flagellates are limited to the mid gut and as a rule died out in three or four days unless the flies were re-fed. It is evident that *P. sergenti* is a much less favourable host than *P. major* var. *chinensis* for the parasite of kala azar.

C. M. W.

Hindle (E.) & Patton (W. S.). **Sand-Flies and Chinese Kala-Azar.** [Correspondence.]—*Nature.* 1927. Mar. 26. Vol. 119. No. 2995. p. 460.

In this note the authors record the infection of a hamster with leishmania as a result of intraperitoneal injection of the flagellates which had developed in the mid gut of 5 *Phlebotomus sergenti* var. fed three days previously on an infected hamster. It is evident that the flagellates which develop in sand flies from ingested leishmania are capable of giving rise to infections.

C. M. W.

Arena (G.). Contributo allo studio della patogenesi della leucopenia nel kala-azar infantile. [**The Pathogeny of Leucopenia in Infantile Kala Azar.**]—*Pediatria.* 1927. May 1. Vol. 35. No. 9. pp. 465–475. With 2 charts in text. [13 refs.]

Maggiore and Sindoni claimed that the serum of children suffering from kala azar contains a substance which is leucocytolytic, as evidenced by the diminution of the leucocytes in normal blood when incubated for 2 hours with the serum of kala azar cases. The author of the paper under review has repeated the observation on 7 cases of infantile kala azar and finds that the claims are justified. The presence of the

leucocytolytic substance, however, is not constant as in his series the number of leucocytes destroyed per millimetre of blood varied between 1,400 and 0. The brunt of the destruction falls upon the polynuclears.

C. M. W.

CLAXSON (H. H.). **Does a Species of Leishmania occur in the Goat ?**—*11th & 12th Reports Director Vet. Education & Res.* Dept. of Agric. Union of S. Africa. Part I. 1926. Sept. pp. 29–30. With 1 coloured plate. [2 refs.]

In a blood film made from the ear of a goat which had been used for feeding tsetse flies a group of organisms, illustrated in a coloured plate, and other isolated forms were found. They were regarded as leishmania and the provisional name *Leishmania caprae* was given to the supposed parasite. No further examination of the goat could be made.

[From the coloured plate it appears to the reviewer highly improbable that the organism is a leishmania. The appearance of a group of these organisms in a film of the peripheral blood is most unusual. As it is definitely stated that the distilled water used for staining could not have yielded the organisms it seems most probable that the structures are yeasts and that the blood was contaminated from the skin of the animal. The possibility of their being rounded forms of trypanosomes can hardly be considered as there was no evidence that the goat had any trypanosome infection.]

C. M. W.

BHATTACHARJYA (Subodh Chandra). **An Interesting Case of Kala-Azar.**—*Med. Rev. of Reviews.* Calcutta. 1927. Mar. Vol. 2. No. 3. pp. 124–125.

A case of kala azar in a female patient aged 14 years who was cured by injections of urea stibamine after tartar emetic had failed to control the condition.

BARBACCI (Piero). Un secondo caso di leishmaniosi interna infantile osservato in Siena. **Second Case of Infantile Leishmaniasis in Sienna.**]—*Policlinico.* Sez. Prat. 1927. May 9. Vol. 34. No. 19. pp. 667–671. With 3 text figs. [1 ref.]

A detailed description of a second case of infantile kala azar from Sienna Italy. (See this *Bulletin*, Vol. 23, p. 587).

BROOKE (R.). **Kala-Azar. Report of a Case.**—*Amer. Jl. Trop. Med.* 1927. Jan. Vol. 7. No. 1. pp. 27–38.

A case of kala azar in a young man 28 years of age who was admitted to, the Ancon Hospital from a steamer. The infection appears to have been contracted in or near Calcutta, where the patient had lived for 15 years.

PITTALUGA (G.). **Epidemiological Study of Leishmaniasis Visceralis in Spain.**—*Jl. Trop. Med. & Hyg.* 1926. Dec. 1. Vol. 29. No. 23. pp. 387–398. With one map in text. [Numerous refs.]

This paper is an English version of that reviewed in this *Bulletin*, Vol. 23, p. 576. There is one discrepancy between the two. The present version states that many hundreds of cases of infantile kala azar have been observed in Spain since 1925, whereas in the French version the date given is 1912. The latter is undoubtedly correct.

C. M. W.

Dostrowsky (A.). **A Study of Cutaneous Leishmaniasis in Palestine.**—*Ann. Trop. Med. & Parasit.* 1926. Dec. 17. Vol. 20. No. 4. pp. 385–406. With 3 plates, 1 text fig. & 1 map.

An investigation of the histories of 28 cases of oriental sore contracted in Palestine proves that the disease is present throughout a large area of the country and that the cases come from localities showing marked variations in geographical and meteorological conditions. Thus, the following places supplied cases of the disease :—Jericho, 820 feet below sea level with a tropical climate, Jerusalem, 2,593 feet above sea level with a temperate climate, and Kantara 150 feet above sea level. In a series of 100 cases, 72 of which had been imported from Persia, Mesopotamia and elsewhere, the sores in a single individual varied from 1 to 158. The clinical picture is that well known from the literature on the subject. The Wassermann test made on a small number of cases showed that in the disease changes occur which give rise to a positive reaction. In 65 per cent. of 74 cases from which information was obtained it might be concluded that the lesions first appeared between September and April immediately before and during the rainy season. The family incidence of the disease is also emphasized and it is noted that 24 of the cases were in 7 families. A discussion of the method of transmission of the disease leads to the conclusion that the distribution of the cases and the lesions can be explained on the hypothesis that sandflies are the carriers. The paper is illustrated by 5 excellent photographs of oriental sore.

C. M. W.

Sergent (Edm. & Et.), Foley (H.) & Parrot (L.). Observations statistiques sur le bouton d'Orient en Algérie. [**Statistical Observations on Oriental Sore in Algeria.**] *Arch. Inst. Pasteur d'Algérie.* 1926. Mar. Vol. 4. No. 1. pp. 20–25. With 1 plate. [2 refs.]

A review of the 112 cases of oriental sore seen at the Pasteur Institute of Algeria, during the period 1915–1925, shows that though the exposed parts of the body as commonly understood are most usually affected, the extent of the actual exposure varies with the habits of the people and their behaviour when in hot climates. The occurrence of sores on the body can be accounted for by the custom of certain individuals of sleeping on hot nights without any covering whatever, so that the whole body is exposed to the bites of sand-flies. The ages of the patients showed that in natives the majority were between 1 and 15 years of age, the age 6 to 10 being the optimum. In the case of Europeans, who moreover were more liable to multiple lesions, all ages were afflicted alike. In 47 Europeans the onset of the disease was during the last five months of the year. In one case, three years after the appearance of a sore on the right arm, two sores developed on the face.

C. M. W.

Agronick (M. A.). Beiträge zur Epidemiologie und Kasuistik der Orientbeule. [**Epidemiology and Symptomatology of Oriental Sore.**]—*Dermat. Woch.* 1927. Feb. 19. Vol. 84. No. 8. pp. 261–273. With 3 text figs. [46 refs.]

The paper discusses the subject of oriental sore which is very common in Turkestan and Transcaspia. Four cases are described with a view

to illustrating the family incidence of the disease and the possible involvement of the mucosae, the latter condition being seen in two of the cases which showed involvement of the mucosa of the lips without any ulceration of the neighbouring skin from which extension could have taken place. In both cases there were sores on the skin on other parts of the body.

C. M. W.

Burga (Buenaventura). Distribución geográfica de las leishmaniasis en el Departamento de Amazonas. [**Distribution of Leishmaniasis in Amazonas, Peru.**]—*Cronica Méd.* Lima. 1926. June. Vol. 43. No. 756. pp. 169–174. With 3 text figs.

As regards the distribution of uta in Uctubamba the district is divisible into 3 zones. The first is 2,800 metres above sea level, is cold and is free from the disease; the second, 2,000 metres above the sea, has a temperate climate and here uta is found; while the third with an altitude of 1,000 metres is hot and is characterized by its malaria and ankylostomiasis. A case of the disease in a man 25 years of age is described. There was extensive involvement of the naso-pharyngeal and buccal mucosae and of both feet, the terminal part of one of which was reduced to a granulomatous mass. Treatment with tartar emetic was instituted and though the patient would not continue the course the considerable improvement which took place justified the diagnosis of leishmaniasis.

C. M. W.

Mazza (Salvador). Leishmaniosis tegumentaria y visceral. [**Dermal and Visceral Leishmaniasis.**]—*Bol. Inst. Clin. Quirúrg.* Buenos Aires. 1926. Vol. 2. No. 13. pp. 209–216. With 27 figs.

The article is a general discussion of the subject of cutaneous leishmaniasis in the Argentine and its relationship to the similar disease in dogs and the distribution of sand flies. It is illustrated by a series of photographs showing the parasites from the sore and their cultural forms, several cases of the lesions in human beings and dogs, and sand flies. It is evident the disease is widely distributed. It is of interest to note that in one particular house in which sand flies (*Phlebotomus verrucarum ?*) were captured there occurred five cases of the disease in man and what was undoubtedly one in a dog, though unfortunately the animal was destroyed before a microscopic examination had been made.

C. M. W.

Arias Aranda (Carlos). Un caso autóctono de leishmaniosis cutánea en la ciudad de Salta. [**Indigenous Case of Dermal Leishmaniasis in the City of Salta.**]—*Bol. Inst. Clin. Quirúrg.* Buenos Aires. 1926. Vol. 2. Nos. 14, 15 & 16. pp. 322–326. With 2 text figs. Also in *Semana Méd.* 1927. Jan. 13. Vol. 34. No. 2 (1722). pp. 94–96. With 2 text figs.

The paper describes a case of cutaneous leishmaniasis, the first autochtonous case to be recorded from Salta in the Argentine. The history of the case is of interest as the patient, a woman 30 years of age, gave a definite history of having been bitten on the arm by an insect

which she described as being much smaller than a mosquito. The mark of the bite rapidly developed into a lesion which did not respond to simple treatment. It was 3 centimetres in diameter by the 6th day. It increased in size and was associated with pains in the finger joints and axillary glands. Finally leishmania were found in scrapings from the sore about one month after the bite. Intramuscular injections of Spirby's mixture, the chief constituent of which was double iodide of bismuth and quinine, were given on 14 occasions during the next eight weeks, with the result that complete healing took place.

C. M. W.

Bernasconi (Vicente E.) & Paterson (Guillermo C.). Observaciones ilustrativas de las formas de espundia en el norte de la República. [**Muco-Cutaneous Leishmaniasis (Espundia) in the Northern Parts of Buenos Aires.**]—*Bol. Inst. Clin. Quirúrg.* Buenos Aires. 1926. Vol. 2. Nos. 14, 15 & 16. pp. 327–347. With 36 figs.

This brief paper is illustrated by 36 photographs, which give excellent representations of the condition. The chief points of interest are that in many cases there is seen a primary lesion of the skin where an insect has implanted the virus. This heals spontaneously, the mucocutaneous lesions being of the nature of a secondary stage to this "espundial chancre," which is probably present in all cases, but may be quite small and masked by the later destructive changes. Affections of the palate and pharynx are metastatic since these sites are inaccessible to the bites of insects. The author states in support of this that in no case where the primary lesion has been treated with tartar emetic has espundia followed.

H. Harold Scott.

Adler (S.). **A Note on the Histopathology of a Case of Experimental Cutaneous Leishmaniasis.**—*Ann. Trop. Med. & Parasit.* 1926. Dec. 17. Vol. 20. No. 4. pp. 407–410. With 1 plate.

As a result of inoculation of an individual with the naturally occurring flagellates of *Phlebotomus papatasii* by scarification of the skin there developed a hard subcutaneous nodule from which leishmania were obtained by puncture. As this lesion differed from the cutaneous ones usually seen in oriental sore a portion of the nodule together with the overlying skin was removed for histological study. The nodule was found to be 4·5 mm. in diameter in cross section while the outer surface of the epidermis was 2·5 mm. distant from the nearest point in the nodule. The lesion itself was not encapsuled and consisted of a conglomeration of tubercles separated from each other by strands of connective tissue infiltrated with lymphocytes, plasma cells and endothelial cells. The tubercles were of varying stages of development, some showing advanced fibrosis and several caseation. Giant cells were a marked feature of the lesion. It is interesting to note that though the inoculation was performed by scarification the epidermis was normal, the flagellates having reached 4·5 mm. below the surface of the epidermis to give rise to the nodule. The corium did show scattered areas of infiltration consisting mainly of fibroblasts with some small round cells and plasma cells, but an absence of endothelial and giant cells. It is concluded that these changes in the corium must have been caused by the trauma incidental to the frequent examinations of the lesion.

C. M. W.

Scanlon (R. W.). **A Case of Naso-Pharyngeal Leishmaniasis.**—*Somaliland Protectorate Ann. Med. & San. Rep. for Year ending 31st December, 1925.* pp. 35–36.

The patient, who had suffered from the disease for 3 years, showed a swelling of the alae nasi and the right cheek. It was found that the nasal septum had necrosed as far as the bony parts and the turbinates had disappeared, leaving one huge cavity covered with granulation tissue. A granular mass occluded the posterior nares while the posterior wall of the pharynx was covered with a friable and vascular adenoid growth. There was enlargement of the sub-maxillary glands. Scrapings from the ulcerated margins showed scanty but typical leishmania. Under treatment with intravenous tartar emetic and Von Heyden 471 and local applications the patient was cured. The author states that he has seen 4 other such cases, 2 of which, as far as he is aware, had never left the protectorate, but it was only in the case described that leishmania were found.

C. M. W.

de Rezende (Mario Ottoni). Cura da leishmaniose das mucosas. Casuistica. [**Treatment of Leishmaniasis of the Mucous Membranes.**]—*Bol. Soc. Med. e Cirurg. de S. Paulo.* Brazil. 1925. Mar., Apr., May & June. Ser. 3a. Vol. 8. Nos. 1, 2, 3 & 4. pp. 76–81.

The author recalls the fact that in 1923 he placed on record a form of treatment of muco-cutaneous leishmaniasis by lactic acid, illustrated by two cases.

Another 18 cases are now detailed. The principle of the treatment is as follows: Under anaesthesia the affected site is thoroughly curetted and an 80 per cent. solution of lactic acid is applied. This is repeated weekly and in most a second and even a third curettage is carried out at intervals of not less than three weeks. Cure resulted in several cases in a month, and in most within 3–4 months.

In some patients lactic acid was injected intravenously, 2 cc. of a 1 per cent. solution at first, later a 2 per cent. solution. Originally this was administered every two days, but every 8 or even 10 days was found preferable. Headache, dyspnoea, and pain in the chest were indications for suspending the treatment, and the local application of the strong solution, 80 per cent., has given much better results.

H. Harold Scott.

Varma (R. L.). **Berberine Sulphate in Oriental Sore.**—*Indian Med. Gaz.* 1927. Feb. Vol. 62. No. 2. pp. 84–85.

The author, having heard that local applications of rasout—a dry extract of *Berberis indica* –were of benefit in oriental sore, tested the action of berberine sulphate [0·25 gr.—? gram or grain] in 1 cc. distilled water injected into the sore by means of a hypodermic syringe. In the first case this treatment produced local reaction in the form of congestion and oedema, but associated with little pain or tenderness. A week later the sore was again infiltrated with the solution. The patient was entirely cured and did not require a third injection. The method

of treatment has since been followed in many cases so that the author is led to believe that berberine is as specific for oriental sore as quinine for malaria.

C. M. W.

Adler (S.) & Theodor (O.). **The Identity of *Leishmania tropica* Wright, 1903, and *Herpetomonas papatasii* Adler, 1925.**—*Ann. Trop. Med. & Parasit.* 1926. Dec. 17. Vol. 20. No. 4. pp. 355–364. With 2 plates. [19 refs.]

The authors have previously reported that they were able to produce lesions in three persons by the inoculation of the naturally occurring flagellates of *Phlebotomus papatasii*. The parasites in the lesions appeared to be identical with *Leishmania tropica* and there was reason to suppose that the disease produced was actually oriental sore. Nevertheless, since various authors had claimed to have infected vertebrates with insect flagellates which could not possibly be *Leishmania tropica*, it seemed advisable to test the serological relationship of the flagellates cultured from the experimental lesions to those obtained from naturally occurring oriental sore by the method devised by Noguchi. The culture medium employed was agar, 1 part, Locke's solution containing 0·2 per cent. of dextrose, 8 parts, and fresh rabbits' serum, 1 part. If the medium be made with serum from an immunized rabbit or if immune serum be added to a culture already commenced, instead of growing in a uniform layer at the top the organisms grow in clumps for a varying distance throughout the medium. Rabbits were immunized with the flagellates grown from the three experimental cases and with those from three cases of oriental sore and their sera tested against the cultures by the above method. The cultures were also tested by Kligler's method which consists in mixing one part of culture with six parts of saline and centrifuging. The supernatant fluid is removed and fresh saline added. The process is repeated three times when a uniform suspension of flagellates is obtained. With this suspension agglutination may be performed in test tubes by adding immune serum to any required dilution. The tubes are read after 24 hours. After reading they are shaken, and it will be found that if agglutination has taken place, a uniform suspension cannot be made. Agglutination was produced in dilutions varying from 1 in 100 to 1 in 500.

The tests proved that the six strains of flagellate were serologically identical so that there can no longer be any doubt that *Herpetomonas papatasii*, the naturally occurring flagellate of *Phlebotomus papatasii*, is identical with *Leishmania tropica* and that the last name is the correct one for the flagellate whether found naturally in the fly or in oriental sore.

C. M. W.

Adler (S.) & Theodor (O.). **The Behaviour of Cultures of *Leishmania tropica*, *L. infantum*, and *L. braziliense* in the Sandfly, *Phlebotomus papatasii*.** [Correspondence.]—*Nature.* 1927. Jan. 8. Vol. 119. No. 2984. pp. 48–49.

& —. **The Behaviour of Cultures of *Leishmania* sp. in *Phlebotomus papatasii*.** [Correspondence.] *Ibid.* Apr. 16. No. 2998. p. 565.

The authors have found that sand flies (*P. papatasii*) may be as readily infected with *Leishmania tropica* by feeding them on cultures of

the organism through a membrane of rabbit skin as by the ingestion of leishmania from an oriental sore. The short sojourn of such culture forms in the fly would appear to increase their virulence, for the flagellates from such a fly which had died on the eleventh day (September 26th) after feeding on a culture were inoculated by scarification to the skin of the arm of a volunteer who was at the same time similarly inoculated at two spots on the other arm with flagellates from the same culture. By November 1st a papule containing leishmania had developed at the site of inoculation by the flagellates from the fly but up to November 16th, nothing had appeared on the other arm. The infection of sand flies from cultures of *Leishmania tropica* led to experiments with cultures of other species, viz., *L. infantum*, and *L. brasiliensis*. It was noted that in the flies they behaved quite differently from *L. tropica*. Though active division and, in the case of *L. brasiliensis*, marked morphological changes occurred the flagellates were confined to the stomach though in 2 out of 20 cases in *L. brasiliensis* they were also found in the lowest part of the cardia. In no case did they pass to the uppermost part of the cardia nor were any forms found attached to epithelium. It would appear that the invasion of the upper part of the cardia and the attachment to the epithelium which occurs in the case of *L. tropica* in *P. papatasii* and *L. donovani* in *P. argentipes* are indications that these flies are the actual transmitters. Should these observations be repeated with recently isolated cultures of *L. infantum*, it would be justifiable to assume that *P. papatasii* is not the vector of Mediterranean kala azar.

In the second note the authors point out that by error it was stated in the first that the fly from which the case mentioned was inoculated, was a " laboratory bred " fly. This was not the case, the insect being a wild one caught in Jerusalem. As the incidence of natural infection of flies in Jerusalem is either nil or so small as to be negligible the conclusion as to the source of the flagellates in the fly is not invalidated

C. M. W.

WATANABE (K.). Beitrag zur Kenntnis der Leishmaniosis cutanea. [**Study of Dermal Leishmaniasis.**] - *Japan Jl. Dermat. & Urol.* 1926. Nov. Vol. 26. No. 11. German summary pp. 63–66. With 2 figs. on 1 plate. [In Japanese pp. 999 1020. With 5 text figs. 139 refs.]

As Japan is not an endemic centre for cutaneous leishmaniasis the only cases met with in the country are imported. Such a case in a man who had resided for some years in Bolivia is recorded. He had an infection of the right ear. With material from the lesion a series of animals was inoculated in various ways. A rat inoculated intraperitoneally developed two nodules on the back and one on the neck ; another rat similarly inoculated developed nodules on the face, neck and back, and acquired a generalized infection ; a third rat intraperitoneally inoculated developed an ulcer on the left shoulder, while a rabbit inoculated in the right eyelid with material from one of the nodules in the first rat, developed ulcers on the upper and lower jaw, a nodule at the left angle of the mouth and another on the floor of the mouth. Leishmania were demonstrated in all these animals.

C. M. W.

Parrot (L.) & Donatien (A.). Leishmaniose cutanée primitive expérimentale de la souris blanche. [**Experimental Primary Cutaneous Leishmaniasis of the White Mouse.**]—*C.R. Soc. Biol.* 1927. Feb. 25. Vol. 96. No. 7. pp. 448–449.

It is pointed out that if mice are inoculated in the skin of the tail at 2 or 3 points with a few drops of culture of *Leishmania tropica*, in 8 to 10 days small nodules rich in leishmania will develop. Around these nodules the skin becomes infiltrated and finally ulceration with the formation of scabs occurs. In some cases the ulceration will extend till the whole tail, which may drop off, becomes involved. As a rule the mice remain in good general condition, and retain the infection for as much as 15 months. When the ulceration has been extensive, however, the animals ultimately become cachectic and die of a secondary bacterial infection. In such cases the spleen is either not enlarged or only slightly increased in volume and shows a scanty leishmania infection. The infection can be handed from mouse to mouse by inoculation of serum from the tail.

C. M. W.

Messik (R. E.). Ueber Thrombozytobarine gegen *Amoeba endolimax* und *Leishmania tropica*. [**Thrombocytobarine against Amoeba and *Leishmania tropica*.**]—*Cent. f. Bakt.* I. Abt. Orig. 1927. Feb. 5. Vol. 101. No. 6–7. pp. 413–417. [10 refs.]

———. Ueber die Trombocytobarine gegen der Amoeba Endolimax und Leischmania Tropica.—*Arb. a. d. Microbiol. Inst. d. Volksunterrichtskomissariats.* 1926. Vol. 2. German summary p. 210. [In Russian pp. 194–210. 10 refs.]

The presence of a substance, thrombocytobarine, in immune sera and its property of causing blood platelets to adhere to spirochaetes and trypanosomes has been shown by various authors to be a specific reaction. The present writer has immunized mice by injections of cultures of *Leishmania tropica* and a free-living amoeba termed *Amoeba limax*. The development of thrombocytobarine in the animals injected with leishmania was demonstrated but not in those injected with the amoebae. In the case of the leishmania-immunized mice, the thrombocytobarine remained in the blood for 3 to 6½ months. The substance was not found in the blood of young animals born of an immunized parent.

C. M. W.

Jessner (Max). Wie sind die Aussichten einer Immunisierung gegen Hautleishmaniose und einer Therapie der Erkrankung mit Leishmaniavakzine? **Prospects of Immunization and Treatment of Dermal Leishmaniasis by Leishmania Vaccine.** *Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Feb. Vol. 31. No. 2. pp. 72–74.

The author is surprised that the possibility of vaccine therapy in leishmania infections has not attracted more attention. Apart from certain experiments of Nicolle and Mancaux (1910, 1911) and Row (1912) very little has been done. In a previous note (this *Bulletin*, Vol. 22, p. 686) the author in collaboration with Amster called attention to the fact that a definite skin reaction followed the injection of a vaccine into the skin of the dog and man, during or after recovery from *Leishmania tropica* infection. Attention was then directed to the possibility

of employing the vaccine for purposes of immunizing against the infection. Dogs were used but, owing probably to the shortness of the time during which they were subjected to injections of vaccine, no immunity was produced. It was discovered, however, that dogs which had recovered from an infection were not immune to a second inoculation. The disease in dogs was, however, definitely influenced by vaccine treatment, the lesions ceasing to develop and healing more rapidly than in the controls.

The author suggests that the investigations are well worth pursuing in the case of human beings in countries where the disease is endemic.

C. M. W.

Chadwick (C. R.) & McHattie (C.). **Notes on Cutaneous Leishmaniasis of Dogs in Iraq.**—*Trans. Soc. Trop. Med. & Hyg.* 1927. Mar. 9. Vol. 20. No. 7. pp. 422–432. With 28 figs. on 3 plates. [27 refs.]

Oriental sore is very common in dogs in Bagdad and other parts of Iraq, and one of its most notable features is its seasonal incidence. During the cold months affected dogs showing raw, repulsive-looking sores on the nose and about the eyes may be seen in any street or bazaar; yet, during the summer months, one may search Bagdad from end to end, and not be able to find a single case. During the period January 1st to May 30th, 1926, 28 cases diagnosed microscopically were encountered. Cases were seen in Bagdad, Mosul, Nasiriya, Baquba, Hillah, Amarah, Kirkuk and Khanaqin. As in man the disease attacks the exposed parts of the body—nose, lips, eyelids, internal surface of ears, toes, pads and other parts. The condition appears to be a purely local one as careful examination of the internal organs of certain cases, failed to reveal any generalized infection. The parasite from the sores appears to be identical with *Leishmania tropica* of human oriental sore. Canine kala azar does not appear to exist in Bagdad, as the examination of 130 dogs which were destroyed did not yield any case of this infection. Treatment of the canine oriental sore is useless, the disease running its natural course of nine months. The paper is illustrated by a series of photographs, showing the parasite and the lesions it produces.

C. M. W.

i. Sergent (Et.), Gueidon (E.) & Pagès (A.). Chronique du bouton d'Orient en Algérie (24e, 25e, et 26e, cas en dehors de la région saharienne). **Oriental Sore in Algeria.**—*Arch. Inst. Pasteur d'Algérie.* 1926. Mar. Vol. 4. No. 1. pp. 26–29. With one map in text. [5 refs.]

ii. Bertrand (M.). Un nouveau cas de leishmaniose cutanée dans le Tell.—*Ibid.* p. 30. With 1 plate.

iii. Boisseau (A.). Sur un cas de bouton d'Orient contracté dans la région de Laghouat.—*Ibid.* pp. 31–34. With 1 plate.

i. A record of three further cases of oriental sore from the Tell district in the north of the department of Constantine.

ii. A case of oriental sore from the same region.

iii. A case of oriental sore in the south of the department of Algeria.

C. M. W.

Gray (A. M. H.). **Case of Leishmaniasis.** *Proc. Roy. Soc. Med.* (Sect. of Dermat.). 1926. Dec. Vol. 20. No. 2. p. 102.

A case of oriental sore in an Indian student who first showed signs of the infection six months after his arrival in England.

de Mello (Froilano) & Camotim (V.) Premier cas autochtone de bouton d'Orient à Goa. [**First Case of Oriental Sore contracted at Goa.**] *Arquivos Indo-Portugueses de Med. e Historia Nat.* Nova-Goa. 1926. Vol. 3. p. 296. With 1 fig.

The record of a case of oriental sore in a soldier stationed at Margao, where the infection appears to have been acquired. This is the first case of the disease to be noted from Goa.

Sergent (Edm. & Et.), Parrot (L.), Donatien (A.) & Béguet (M.). Observation et iconographie d'un clou de Biskra transmis par *Phlebotomus papatasi* (Scrop.). Etude expérimentale du virus.—*Arch. Inst. Pasteur d'Algérie.* 1926. Mar. Vol. 4. No. 1. pp. 1–19 With 24 figs. on 14 plates. [15 refs.]

With the addition of a few more photographs, this paper is the same as that by the authors reviewed in this *Bulletin, ante*, p. 140.

Aragão (Henrique). Palestra sobre Leishmanioses. [**Concerning Leishmaniasis.**]—*Sciencia Med.* 1927. Mar. 31. Vol. 5. No. 3. pp. 121–132. With 3 text figs. & 3 plates.

A general account of present knowledge on the subject of cutaneous leishmaniasis.

Mazza (Salvador). Consideraciones sobre flebótomos encontrados en Tabacal y el papel de estos dipteros en la transmisión de las leishmaniosis. **Phlebotomi met with in Tabacal and their Rôle in the Spread of Leishmaniasis.** *Bol. Inst. Clin. Quiming.* Buenos Aires. 1926. Vol. 2. Nos. 14, 15 & 16. pp. 310–317. With 8 text figs. [5 refs.]

After a preliminary dissertation on the present state of knowledge of the relationship of sandflies to cutaneous leishmaniasis an account is given of certain members of the genus *Phlebotomus* which were captured at Tabacal, in the Argentine, presumably from the point of view of their possible connexion with the cutaneous leishmaniasis of that country.

C. M. W.

Monier-Vinard. Le kala azar : étude clinique et thérapeutique.—*Rev. Prat. Malad. des Pays Chauds.* 1926. Jan. Year 4. Vol. 5. No. 8. pp 391–407.

BLACKWATER FEVER.

i. Manson-Bahr (Philip) & Sayers (Edward G.). **Blackwater Fever in London. A Critical Study.**—*Lancet.* 1927. Feb. 5. pp. 273–277. With 1 chart in text. [16 refs.]

ii Greene (E. F.). **Blackwater Fever in England.** [Correspondence.] —*Ibid.* Mar. 12. pp. 568–569.

i. This paper is based on an analysis of 14 cases of blackwater fever which have developed in London during the last seven years. All the patients were Europeans who had returned from service in Africa, especially the West Coast, i.e., Nigeria 6, Gold Coast 3, Belgian Congo 2, Kenya 2, and N. Rhodesia 1. The length of sojourn in the endemic area varied in 11 cases from one to five years, average 3·2 years. In no case did blackwater develop later than 10 weeks after arrival in England; the average time was 4 weeks. The reacclimatization period is the period of danger. Antecedent syphilis seems to play no part, and the Wassermann reaction was performed in 5 instances before the onset of blackwater with negative results. In only one case was there a definite history of alcoholic excess. Sex and age appeared to have no influence on the incidence of the disease. The mortality rate in the authors' series was 50 per cent., which compares unfavourably with the average 23·5 per cent. worked out by Thomson in over 1,000 cases in Rhodesia [this *Bulletin*, Vol. 22, p. 414.]

The relationship of the disease to malaria was carefully investigated, and the findings are in entire agreement with those of Thomson. The evidence on this point is considered under three headings–endemic area, clinical history of subtertian malaria, and parasitic findings. Subtertian rings were found in 50 per cent. of the cases, and, considering that many of the patients came under observation only after the onset of blackwater, this is by no means a low proportion. A table is given correlating the parasite findings with the day of the disease.

Turning to the relationship of quinine to blackwater fever the authors state that they were unable to confirm entirely the statement of Thomson that he had not seen a single case of blackwater in a person who had taken 5 grains of prophylactic quinine daily. Amongst their 14 cases 2 took 5 grains daily during their stay in Africa and also during the voyage to England, another had taken regularly 15 grains every Saturday and Sunday, and finally a child aged 3½ years had been given 2 grains of quinine daily since leaving the endemic area and during her stay of two months in England.

In this series of 14 cases it is difficult to escape the conclusion that quinine is a potent factor in precipitating the crisis: in all cases save one quinine had been given just prior to the attack, the doses varying from 5 to 28 grains daily. Details are given of several cases in which chill seemed to play a part as a precipitating factor.

After considering the clinical aspects and physical signs exhibited by their patients the authors turn to the urine. Minute observations of the urine were made only in two cases before the onset of blackwater. In one the only abnormality was a trace of albumen two hours before the onset, and in the other the urine was normal the day before the attack, but six hours before it contained urobilin and urobilinogen and also albumen and granular casts. The time of onset was usually in the early

morning and the average duration 2·8 days (1 to 4 days). Suppression was not a marked feature in this series, two cases only exhibiting it. Bile was never found in the urine.

The observations on the blood are in agreement with those of other investigators. Before the attacks the picture is that of a severe case of subtertian malaria. In one case which recovered the red cells dropped to under a million per cmm. and the haemoglobin to 10 per cent. "A simple clinical observation regarding the presence of haemoglobinaemia was made in several cases." At the commencement of haemoglobinuria the colour-index is relatively high (in one case 1·5), but later it falls to normal or below it. The authors suggest that the high percentage of haemoglobin in the first instance is explained by the presence of free haemoglobin in the serum. [This is obviously an important question, but unfortunately, beyond the quite indefinite statement quoted above in inverted commas, no information is given regarding the presence or absence of haemoglobinaemia].* In only one case (fatal) were parasites extremely numerous. The cause of death in the seven cases was septic parotitis 1, acute cardiac failure 1, acute haemolysis 4, and pneumonia 1.

With regard to treatment the authors lay down certain broad principles. In the pre-blackwater stage the specific treatment of the subtertian malaria should be commenced with small and repeated doses of quinine, e.g., 1 grain at four-hourly intervals, gradually increasing the dose as tolerance is established. Every precaution should be taken against chill. As all work indicates that suppression is less likely to occur if the urine be alkaline, massive doses of potassium citrate, either alone or with sodium bicarbonate, should be given until the urine is alkaline; in most cases oral administration will suffice. During haemoglobinuria the urine, if not already made alkaline, as above, should be made so by the intravenous injections of sodium bicarbonate (150 grains to 1 pint of distilled water) as recommended by Hanschell. Not more than a pint should be given at a time owing to the very real danger of oedema of the lungs. Regarding the question of administration of quinine when once blackwater has commenced, the view is expressed that there is no evidence that the continued administration of the drug has any appreciable effect on the disease.

In cases with severe haemolysis the question of blood transfusion from a suitable donor is worth consideration and the authors are encouraged by the results obtained in one case.

The remainder of the paper is concerned with the theory of the genesis of blackwater fever based upon a study of these cases correlated with recent biochemical knowledge. That in subtertian malaria haemolysis occurs with each attack of fever is evident from the following facts: (1) progressive anaemia; (2) indirect positive van den Bergh reactions with the serum; (3) the presence in the urine of urobilin in pathological amounts; and (4) excessive formation of bile leading to bilious vomiting. The haemoglobin is split up into haematin (the iron-containing part) and globin (the iron-free protein part). It is generally maintained that haematin is gradually split up by the

* Dr. Manson-Bahr writes to the Editor:—"That haemoglobinaemia of an appreciable degree, easily detectable by the naked eye and by the spectroscope, was present was proved by two cases, in which 1 cc. of blood was abstracted and centrifuged directly after the onset of blackwater. The serum was tinged a cherry-pink and gave the spectroscopic bands of oxyhaemoglobin. The sentence containing this information has dropped out of this paragraph in setting up the type in our paper. I regret the omission."

reticulo-endothelial system into : (1) an iron-free pigment haematoidin, or bilirubin, and (2) an iron-containing pigment, haemosiderin. The bilirubin is excreted by the liver, resulting in an increased flow of bile ; the liver, however, is unable to deal with the urobilin, which is absorbed from the intestine and therefore appears in the urine. At the same time the amount of bilirubin in the blood is increased. So long as the liver is functioning well, no bile will appear in the urine, because of the relatively high renal threshold in haemolytic jaundice which admits of the possibility of between 5 to 18 units in the serum without the appearance of bile in the urine. This is the probable explanation of the discoloured skin and lemon-tinted sclerotics which characterize subtertian malaria.

The haemosiderin is deposited as brown or yellowish-brown granules in the liver, spleen, bone-marrow and kidney, from which it is later taken up to be utilized in the formation of new red corpuscles. In the majority of cases of subtertian malaria there is little or no haemoglobinaemia, but in a severe infection the reticulo-endothelium cannot deal with all the haemoglobin and a certain degree of haemoglobinaemia results. It is only when haemoglobinaemia reaches a certain level that haemoglobinuria occurs, because the kidneys have a definite threshold for haemoglobin.

After referring to the work of Baker and Dodds (see below, p. 664) the authors pass to a theoretical explanation of haemolysis. They believe that blackwater is invariably associated with subtertian malaria ; those cases in which *P. vivax* only have been found are regarded as double infections, and those which have developed in the course of the malarial (*P. vivax*) treatment of general paralysis are dismissed 'without the slightest evidence' as really cases of paroxysmal haemoglobinuria. Haemolysis occurs in the spleen pulp and capillaries of the internal organs and coincides with the full development of schizogony of *P. falciparum*. It is possible that in blackwater full development of schizogony of a very large number of parasites might be obtained at the same moment. The haemolysis in the spleen would then be extreme and the amount of free malarial haemolytic toxin liberated proportionately great. The absorption of this sudden massive dose of malarial toxin into the general circulation leads to general haemolysis. [If this be so, one would expect that the presence of this haemolytic substance might have been recognized ere now by *in vitro* observations.]

There are two possible ways in which quinine may act in the production of blackwater. It has been shown by Kingsbury that the administration of quinine in subtertian malaria is always followed by an increase in the serum bilirubin. This means that quinine causes definite haemolysis of the infected red cells, and it is conceivable that this increased haemolysis might just be sufficient to precipitate the onset of blackwater.

There is evidence that quinine can cause contraction of the spleen by a specific action on the non-striped muscle of that organ (Cushny, 1924). A sudden contraction of a heavily-infected spleen, even if only of very short duration, would force a very large amount of haemolytic toxin into the general circulation, and might thus cause a profound haemolysis.

ii. The author writes that while it is impossible to controvert much of the theory in the above paper, there are almost epidemic forms of blackwater that do not harmonize with the subtertian causation. The author believes that the blood picture in subtertian malaria is

essentially different from that seen in blackwater; he considers that the whole question is most important, because it raises the point whether quinine should or should not be administered for severe malaria; good results can be obtained from phenacetin in malaria and possibly with less danger. [A statement like this seems in the present state of knowledge to be a dangerous doctrine and unjustifiable unless supported by adequate data dealing with the action of phenacetin in *P. falciparum* infection.] The author likewise has doubts about the value of quinine as a prophylactic and mentions that he himself has had two severe attacks of malaria notwithstanding the fact that he has always taken quinine religiously whilst in W. Africa.

The letter concludes as follows :—

"During five years' work on the coast of Africa, I had always a microscope at hand with me and examined every blood-infected case that I had to deal with. I never saw any other medical man using a microscope in daily practice, except in the hospitals of Free Town, Accra, Calabar, and Lagos. The medical officer in Africa ordinarily has not the time at his disposal for much microscope work."

[This is a terrible and, one must hope, unwarrantable indictment. How any man can practise conscientiously in the tropics without constant recourse to a microscope, it is impossible to conceive.]

W. Yorke.

Macmillan (R. J. A.). **Report on Blackwater Fever in Uganda for 1925.** – *Uganda Protectorate Ann. Med. & San. Rep. for the Year ended 31st December,* 1925. pp. 67–69.

During the year 1925, 81 cases of blackwater fever were treated in Uganda and of these 22 ended fatally.

In considering the distribution of these cases, the author points out that although there is an increase in the number in Buganda and the Eastern Province, this is probably due to the fact that the European and Asiatic populations have greatly increased in these two provinces. The greatest number of cases occurred in July when the weather was wetter and colder than usual; the smallest number occurred in March and October, when the weather was warmer than usual.

The greatest incidence of malaria was in June and the smallest in February. Ten of the patients were Europeans and three died; 71 were Asiatics and 19 died. Information is given regarding the age, sex, and length of residence in the Tropics. Of the 81 cases, 25 had had previous attacks of blackwater. It is considered that malaria is undoubtedly the predisposing cause, every patient having previously suffered from this disease. The records suggest that almost anything will precipitate an attack of blackwater fever, e.g., worry, chill, over exertion, quinine, alcohol, etc. Information is given regarding the quinine habits of the patients. Ten are stated to have taken quinine regularly as a prophylactic and 53 to have taken it irregularly. In 13 cases the blood was examined prior to the attack, and in 7 cases parasites were found, six being *P. vivax*, and one a mixed infection of *P. vivax* and *P. falciparum*. Of the 56 cases examined during the attack, 25 were positive, 16 showing *P. vivax* and 9 a mixed infection of *P. vivax* and *P. falciparum*. Information is given in a table of the duration of the haemoglobinuria in 74 cases. The cause of death in the 22 cases was as follows: Cardiac failure 17, suppression and cardiac failure 2, suppression and uraemia 2, exhaustion 1.

W. Y.

Weselko (Otmar). Sulla emoglobinuria da malaria nel distretto della Stazione antimalarica di Scardona (Dalmazia) e sul suo trattamento con calcio e peptone. **Malarial Haemoglobinuria in the District of the Antimalaria Station of Skradin (Dalmatia) and its Treatment with Calcium and Peptone.** —*Riv. di Malariologia.* 1926. Sept.-Dec. Vol. 5. No. 5–6. pp. 653–659. With 1 chart & 1 map in text. [English summary p. 739.]

In Dalmatia, there are places where cases of malaria and blackwater fever occur annually, and in the district of Scardona 49 cases of blackwater have been noted between 1922 and the end of 1926. The local distribution of these cases is shown in a table from which it appears that Dubravizze is the main focus; it is remarked that subtertian malaria is also most prevalent in this place. Of the 49 cases, 24 occurred during the year 1924, and the author considers that this was possibly, in part, due to lack of proper nourishment.

All the patients gave a history of malaria; the duration of the malaria had apparently no influence on the blackwater fever, four cases of this disease occurring after the third attack of malaria.

In a table is given what the author regards as the immediate cause of the attack in the 49 cases; in the great majority it was a dose of quinine in some form or another. The symptoms exhibited by the patients are summarized and this is followed by a discussion on treatment. The first cases were treated as recommended by Matko with disodium phosphate, but this method was soon abandoned as the results were unsatisfactory. Weselko believes that in blackwater fever two pathogenic factors have to be considered: firstly a change in the ionic equilibrium, in which calcium deficiency is the main alteration, and secondly, an increase of complement caused by quinine or other agents. Acting on this hypothesis he tested the therapeutic value of calcium either by the mouth or intravenously, combined with intramuscular injections of Witte's peptone (10 cc. of a 5 per cent. solution up to 3 injections daily). The results are stated to have been good.

W. Y.

Emile-Weil (P.) & Stieffel. Recherches cliniques sur l'hémoglobinurie. **Clinical Researches on Haemoglobinuria.** —*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1926. Apr. 22. Year 42. 3rd Ser. Vol. 50. No. 13. pp. 587–596. [2 refs.]

The question of haemoglobinuria in general and of paroxysmal haemoglobinuria in particular still remains obscure notwithstanding all the work that has been done. Haemoglobinuria *a frigore* is regarded as a special disease, and Donath and Landsteiner's reaction has been considered as pathognomonic of it. The authors describe in detail two cases which exhibited haemoglobinuria without exposure to cold, but in whom the Donath and Landsteiner reaction was unquestionably positive.

From their study of these two cases, the authors lay stress on a number of points:—

1. *The pulmonary symptoms of the haemolytic crisis.* These consist of air hunger and a sensation of cervical and thoracic constriction with dyspnoea; sometimes there are violent fits of coughing. Similar signs have been observed after transfusion of blood. One of the patients had frequent asthmatic attacks.

2. *The frequency of haemoglobinuria: the unrecognised haemoglobinurias.* It is current opinion that haemoglobinuria is a rare condition. This is true of the severe attacks, but with regard to mild forms its truth is doubtful. In the course of a year the authors have discovered by careful examination, four cases of haemoglobinuria, and of these only one was sent to hospital as an example of this disease. The authors believe that these cases escape notice because in the first place they are confused with haematuria, and in the second place because latent haemoglobinuria is difficult to recognize if one is not on the look-out for it. Instances of each class of case are given.

3. *The identity of haemoglobinuria* a frigore *and the other haemoglobinurias, infective and toxic.* The authors pass to a consideration whether more than one factor can precipitate in any case an attack of haemoglobinuria. They quote the interesting case of Roch and Liengme (1922) who whilst studying a patient suffering from true haemoglobinuria *a frigore* found that an attack could be precipitated by an intravenous injection of casein, or by the oral administration of 10 gm. of sodium chloride. Turning to the authors' two cases it is noticed that the first never suffered from any sensation of chill so characteristic of haemoglobinuria *a frigore*, but was probably an infective case since the haemoglobinuria was complicated by signs of acute pulmonary congestion, and bacteriological examination of the urine showed the existence of a Gram-positive encapsulated diplococcus. In the second case no definite cause of the haemoglobinuria was discovered; the case was one of benign purpura. It is emphaized that both subjects gave the serological reactions of haemoglobinuria *a frigore* and that although the initial crises were not produced by exposure to cold, yet such exposure was capable of producing attacks. It is further noticed that in the first case, small doses of novarsenobenzol sufficed to cause attacks of haemoglobinuria.

The authors think that distinction between the haemoglobinurias should not be made and that paroxysmal haemoglobinuria should not be separated from haemoglobinurias which are not paroxysmal.

W. Y.

Stephens (J. W. W.). **The Haemoglobinurias.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1927. Mar. 9. Vol. 20. No. 7. pp. 401–411. [15 refs.]

The author states that this paper was put together at very short notice, and its scope was consequently determined by the matter he already had and not by deliberate selection. Many of the haemoglobinurias are omitted, e.g., the toxic haemoglobinurias and those due to piroplasmosis, and the haemoglobinuria of blackwater fever is only briefly alluded to, mainly because that subject requires a paper to itself.

The following conditions are dealt with:—

1. *Myoglobinuria.* Muscle contains two pigments. (1) Muscle haemoglobin differing from blood haemoglobin in that its bands are nearer to the red end of the spectrum, and (2) Cytochrome, a respiratory pigment of wide distribution in animals, yeast, bacteria, and plants; in the oxidized condition it gives no bands, but on reduction it shows four bands (at 6035, 5645, 5490 and 5190),

A. Myoglobinuria of the horse. This is seen in horses long stabled on rich food, which undergo sudden exposure to cold or

exertion. The symptoms and pathological appearances are described and it is recorded that MEYER-BETZ (1910) found no haemoglobin in the blood.

B. Myoglobinuria of man. A summary is given of two cases, one recorded by MEYER-BETZ (1911) and the other by GUNTHER (1924).

2. *March haemoglobinuria.* FIEGL (1916) records the result of the examination of persons who had marched 35 kilometres. Of 26 examined, 18 (70 per cent.) had haemoglobinuria and of these, 8 had red cells in the urine, 3 had haemoglobin only in the serum, 2 had haematin only, and 6 had haemoglobin + haematin. A summary is given of 5 cases of this condition described by various authors.

3. *Lordotic haemoglobinuria.* PORGES and STRISOWER (1914) in their case, stated that an attack could be induced by walking even for ten minutes in a pronounced lordotic position, while in the upright or kyphotic position no attack, or only a very delayed one, occurred. FÖRSTER (1919) in his case, found no evidence of this, as in the kyphotic bicycling position attacks also ensued. PORGES and STRISOWER suggest that the splenic vessels are constricted, leading to the development of haemolysis; their patient experienced pain in the left psoas muscle, but they did not especially consider this symptom.

4. *Paroxysmal haemoglobinuria.* This condition is characterized by the existence in the blood of the cold amboceptor or haemolysin. Certain precautions must be observed in performing the Donath-Landsteiner reaction. The coagulation temperature at which the serum is obtained is important; 37° C. is the optimum. Oxalated plasma may give a slight or completely negative reaction, with the usual direct technique (i.e. plasma + red cells kept at 0° C. for a time, and then warming to 37° C.), but it gives a positive reaction with the indirect method (i.e., plasma + red cells kept at 0° C. concentrated in the cold and the plasma removed, complement added to the red cells and warmed to 37° C.) Prolonged cooling for some hours may give a negative reaction. Salt solution may entirely interfere with the lytic action of the complement. Cold amboceptor is sensitive to cold and is destroyed in 18 hours at 0° C. Concentration of the red cell emulsion is important; it should be a maximum and should be prepared at 37° C. The cold amboceptor has a peculiar selective action on the red cells, haemolysing particularly the so-called old cells. The cells of obstructive jaundice are very susceptible to the cold amboceptor. The cold amboceptor acts well on autologous and isologous cells, but not on heterologous cells.

An account is given of the symptomatology, and of the urine and blood. Among the rarer forms of haemoglobinuria mentioned are: Haemolytic jaundice, pernicious anaemia, Raynaud's disease, angio-neurotic oedema, internal haemorrhage, haematuria and specific fevers.

In blackwater fever the amount of haemoglobin passed in the urine in a severe case amounts to some 100 cc. of red cells. Simple calculation shows that this represents only about one-twentieth of the haemoglobin lost. Red cell destruction is not necessarily followed by haemoglobinuria, as is clearly shown by experimental work and the injection of haemolytic substances like toluylenediamin.

Urobilin (or urobilinogen) occurs normally in the urine; it is not secreted continuously in uniform concentration, but, on the contrary, in spurts of relatively high concentration, two or three hours after a

meal. According to SALEN urobilin represents a daily moult of red cells.

The article closes with a reference to the life of a red cell. As a result of certain calculations this is estimated to be from 10 to 40 days.

W. Y.

GHIRON (Mario). Studien ueber die Pathogenese des Schwarzwasserfiebers. [**Studies on the Pathogenesis of Blackwater Fever.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1927. Feb. & Mar. Vol. 31. Nos. 2 & 3. pp. 63–72; 113–125.

The first portion of these papers is concerned with a general review of previous work dealing with such questions as the presence or absence of a haemolysin in the serum; what influence the red cells of the haemopoietic system have on the precipitation of a blackwater fever attack; how far quinine salts can alter the behaviour of the serum and red cells; the significance of the various malaria parasites; the significance of lipoids in combination with quinine; the site of the haemolytic processes; and the mechanism of the origin of blackwater fever. The author gives the following summary of his own observations:

He has worked with the serum of four individuals, who at the time of entering hospital were suffering from a severe attack of blackwater fever.

The serum was withdrawn at the time of arrival and also each three or five days afterwards in order to study its variations.

The blackwater fever serum showed *in vitro* a definite haemolytic power against the red cells saturated with quinine. Of the red cells, which were obtained from patients suffering from various diseases and also from normal persons, those coming from patients with tertian or tropical malaria (whether they had, or had not, been treated with quinine) exhibited in the highest degree the capacity for being haemolysed. Thus, in order to obtain a definite haemolytic effect, the combined action of two factors is necessary: (1) Red blood corpuscles from a malarial source, and quinine; and (2) Blackwater fever serum.

The significance of the haemolytic curve becomes clear:—

(1) From the comparison of the haemolytic curve with the hardly perceptible curve of red blood cells in quinine solution.

(2) From a comparison of the haemolytic phenomena of quininized red cells with those withdrawn from various healthy and diseased persons.

(3) From the part which malaria corpuscles appear to play.

It can thus be concluded that in blackwater fever not only is a haemolysin present, the existence of which is perceived when the red cells have absorbed quinine, but that this haemolysin can, for practical purposes, only be brought into action when the red cells are of malarial origin.

The part played by the constitution of the red cells is not clear, and the results of the author's optical experiments are not sufficient to arrive at a definite judgement.

It is, however, clear that a haemolytic substance is present in every case of blackwater fever, and that this can be demonstrated by the method here described: this haemolysin acts in various concentrations and can disappear from the organism after a certain time.

The characteristics of the reaction are :—

1. A blackwater fever serum with active haemolysin can disclose the presence of a malaria infection in the person who supplies the red cells.

2. Quininized malaria blood cells can make manifest the haemolytic power of a serum, if the serum comes from a person who has had a definite, or latent and clinically incomplete, attack of blackwater fever.

W. Y.

Kondo (Y.). **Investigation on the Genesis of Blackwater Fever.**— *Taiwan Igakkai Zasshi.* (*Jl. Med. Assoc. Formosa*). 1926. Mar. No. 252. English summary pp. 1–3. [In Japanese.]

The author summarizes his observations on 98 cases of blackwater at the Government Hospital in Taito, Formosa ; of these 94 were Japanese and 4 were Formosan-Chinese. *P. falciparum* and *P. vivax* were found in about an equal number, whilst *P. malariae* was only rarely met with. The osmotic resistance of the red blood corpuscles of blackwater fever patients was found to be considerably lower than normal, and this was also the case in respect of the resistance of the red cells to quinine hydrochloride. The haemolytic action of antipyrin, antifebrin, and of alcohol, and the influence of the solar rays, temperature, bile, grape-sugar, haemoglobin, serum and carbonic acid gas upon the haemolytic phenomenon were next considered.

The amount of grape-sugar in the blood of malaria patients is higher during the attacks than in the intervals. Lecithin, which of itself is only a feeble haemolytic agent, increases to a considerable extent the haemolytic action of quinine hydrochloride. The content of lecithin in the blood of malaria patients is, as a rule, much higher than that of healthy persons. Grape-sugar inhibits to some extent the haemolytic action of lecithin.

The symptoms of malarial haemolytic icterus are similar to those of hereditary haemolytic icterus, viz. anaemia, jaundice, enlargement of the liver and spleen, yellowish-brown excreta, urobilinuria, a large proportion of reticulated blood corpuscles and a directly negative, but indirectly positive diazo-reaction of the serum. Cases of blackwater fever, like those of malarial haemolytic icterus, exhibit in their blood a great number of basophilic reticulated red cells. These cells are very sensitive to hypotonic saline and to quinine hydrochloride, and consequently if patients suffering from malarial haemolytic icterus, which apparently is a pre-blackwater fever condition, are given quinine hydrochloride haemoglobinuria is precipitated.

The author believes that the basophilic reticulated red cells are young corpuscles. They are found in anaemia conditions and also in the severe anaemia produced in rabbits by injection of phenylhydrazin hydrochloride. When quinine hydrochloride is given to such rabbits, slight haemolysis results, and this becomes much more intense if artificial icterus is previously induced. The viscosity of the blood in blackwater fever patients is generally lower than normal. Spirochaete-like bodies were found in only a few cases, but other " very small particular granules " occur in considerable abundance.

Dealing with the genesis of blackwater fever, the author considers that the remains of the red cells which have been destroyed by malaria irritate the bone-marrow, and that as a result a large number of basophilic reticulate cells are produced ; then from a number of causes,

e.g. exposure to wet, cold, extreme heat, or intense sunlight, and especially an administration of quinine, sudden haemolysis of the numerous basophilic red cells takes place and blackwater fever results.

W. Y.

Perekropoff (G. J.). Ueber Schwarzwasserfieber. [**Blackwater Fever.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1926. July 1. Vol. 30. No. 7. pp. 284–288.

After briefly reviewing the literature concerning the relationship of malaria and quinine in the genesis of blackwater fever, the author turns to his own observations. He states that he has succeeded in producing haemolysis *in vitro* in six cases: and that, in later work on the artificial cultivation of tertian parasites, he has observed haemolysis in a further six of sixty-two cases. The haemolysis occurred in patients who had not been treated with quinine and consequently this drug does not come into the question. The observations seem to indicate that the parasites themselves possess the haemolytic property, and caused the author to employ quinine in two cases of blackwater fever. The first case unfortunately could not be followed up completely; the second was a person who had tertian malaria, but who had never previously had malaria or taken quinine.

Details of the second case are given, from which it is seen that the patient had developed blackwater fever whilst suffering from tertian malaria. Peruvian bark had no effect either on the malaria or on the blackwater. The administration of quinine (·15 gramme twice daily) brought the attack to an end, the urine clearing, and the parasites disappearing from the blood.

W. Y.

Blanchard (M.) & Lefrou (G.). Considérations cliniques pathogéniques et thérapeutiques sur la fièvre bilieuse hémoglobinurique à spirochètes. [**Clinical Considerations on Blackwater Fever due to Spirochaetes.**]—*Bull. Soc. Path. Exot.* 1926. May 12. Vol. 19. No. 5. pp. 345–352. With 9 charts in text. [6 refs.]

The authors enquire whether the cases of blackwater fever in which spirochaetes are found differ from those in which spirochaetes are not found; and in order to decide the point, they give clinical details of 9 cases of the disease which came under observation at Brazzaville, 4 of them having spirochaetes and 5 of them not having spirochaetes. The temperature charts of the 9 cases, all of which are given, are first considered. In 4 of the 5 cases in which spirochaetes were not found, the temperature rose suddenly to 39° or 40° C. and then fell almost equally quickly; the colouration of the urine followed suit; the haemolytic crisis ended within 48 hours, and convalescence set in. Quite different is the state of affairs in those cases in which spirochaetes were found. The febrile disturbance commences suddenly, but it subsides slowly or persists with oscillations for some time; the urine remains coloured for longer, and only gradually clears. The fifth case without spirochaetes, however, fell also into this category, a fact which shows the difficulty of arriving at a clinical diagnosis.

The authors then pass to a consideration of the other two cardinal symptoms, viz., haemoglobinuria and jaundice. Of the six cases examined when the urine was still coloured, only one exhibited haemoglobinaemia. This was a case in which spirochaetes were not found;

the examination of the cases in which spirochaetes were found and also of one other case in which they were not found was negative. The authors, however, consider this test too difficult and too uncertain for the practical purposes of diagnosis.

Turning to jaundice the authors state that there are three types of icterus, viz., that due to obstruction of the bile ducts, that due to insufficiency of the blood, and that due to insufficiency of the liver. In two cases with spirochaetes the urine contained bile pigments, in one case both bile pigments and salts and in the other case only the salts. The presence of both pigments and salts eliminates the haemolytic origin of the jaundice and the existence of bile salts alone implies hepatic insufficiency. It is concluded that in all the cases with spirochaetes the jaundice is due to hepatic insufficiency, and is related to the presence of spirochaetes in the liver and a consequent hepatic toxaemia. In one case without spirochaetes, bile pigments alone were found in the urine and in another case, neither pigments nor salts. Study of the literature suggests that bile pigments are found only exceptionally in the urine and that consequently the icterus is of the haemolytic type, but, unfortunately, in cases without spirochaetes this is not always so.

The paper closes with some remarks on treatment, but as they relate to so few cases they do not require special notice.

W. Y.

WHIPPLE (G. H.). **The Pathology of Blackwater Fever.**—*Amer. Jl. Trop. Med.* 1927. Jan. Vol. 7. No. 1. pp. 1–14. [1 ref.]

The author recalls that in 1909 he published a paper entitled "Blackwater fever and pernicious malaria in Panama" in a new periodical *Malaria*. This journal ran for two years only, and consequently few libraries possess it. At various times DARLING and others had urged the author to publish his data in one of the recognized journals, and the present paper is evidently the result of this request.

It is surprising to find so few papers giving a careful description of the histological lesions of blackwater fever. The author's material was obtained very shortly after death, and studied under favourable conditions. A detailed account of the morbid anatomy and histology of four cases of the disease is given.

The following is the author's summary of his findings :—

"The kidneys in haemoglobinuria are usually a little enlarged, the surface a deep red or mottled red and yellow, the cortex swollen and stippled with red or black dots looking much like ecchymoses, but in reality due to the haemoglobin in the tubules. The organ may have a yellow or even a greenish tint if the jaundice is very marked. If acute nephritis has supervened the cortex is usually greatly swollen and edematous. The pyramids are a uniform deep purple. Acute nephritis is not a constant finding, and the kidneys in 5 cases out of 9 showed no signs of injury from the presence of the haemoglobin in the tubules. Three cases of combined pernicious malaria and blackwater fever presented no evidence of acute nephritis. The kidneys of pernicious malaria are usually normal, except for a little cloudy swelling, but may show an acute nephritis.

"The spleen is perhaps the organ of greatest interest as it shows such definite changes in all its elements—changes that we are accustomed to associate with a toxemia, comparable to that of diphtheria, septicemia, or even typhoid. The spleen is always enlarged in both diseases (malaria and blackwater fever), and in these cases weighed from 185 to 1,250 grams, perhaps an average of 300 to 500 grams. In blackwater fever the organ

presents a bright red or purple velvety pulp and swollen, opaque, sharply outlined Malpighian bodies. It is usually friable in both diseases. In malaria the spleen pulp is of a dark chocolate colour in acute cases, or a slaty or very dark colour in the more chronic cases, and the Malpighian bodies are inconspicuous. Necrosis may be the striking feature of the microscopical picture of blackwater fever, and in acute cases (1,507 and 1,435) may involve a great part of the pulp and Malpighian bodies. The pulp may show a delicate reticulum of fibrin, many nuclear fragments, polymorphonuclear leucocytes, and huge phagocytes in all sections. The endothelium is almost invariably spared and stains sharply, but the venules may contain numbers of little fibrinous thrombi including leucocytes and large phagocytes. Malarial pigment may be scarce or abundant. The Malpighian bodies in the great majority of cases present a central necrosis indicated by the presence of fibrin, nuclear fragments, polymorphonuclear leucocytes, large phagocytes and edema of the tissues. This necrosis may involve only a small part or almost the entire lymph follicle. Pernicious malaria may show these same necroses, but they are much less in evidence, and more apt to involve the pulp alone. Barker has described similar changes in malaria. The spleen in some cases of acute malaria may show no evidence of necrosis, but enormous amounts of malarial pigment free or enclosed in phagocytes. The number and size of the huge phagocytes which may be so conspicuous depends upon the amounts of malarial pigment and cell necrosis, not upon hemolysis.

" The lymph glands and lymphatic apparatus of the intestines may show similar changes in these two diseases. The picture may resemble that described in the spleen, but the necrosis is less in evidence. The lymph follicles may show central necroses of smaller size, but quite like those in the Malpighian bodies, and the marginal lymph sinuses may be distended with wandering cells and phagocytes of all types. This change depends in great part upon the processes going on in the tissues drained by the respective glands, and is a pretty accurate index of this change. It seems fairly conclusive that the finding of large grains of malarial pigment in the glands at the hilum of the liver and round the head of the pancreas indicates an attack of malaria at some previous time or an attack of long duration. These glands bear the same relation to the liver and spleen that the bronchial glands do to the lungs.

" The bone-marrow is hyperplastic in nearly all cases depending on the duration and severity of the blood destruction. Hyperplasia was absent in one case of pernicious malaria. It is rather remarkable that the marrow shows almost no evidences of cell necrosis ; noted in but two cases. The marrow elements all show hyperplasia, but this reaction is more striking in the red corpuscle groups. In some cases the giant bone-marrow cells (megalokaryocytes) are numerous. The striking feature is a distinct relative increase in eosinophile marrow cells, both mono- and polymorphonuclear cells. This is conspicuous in smears and microscopical sections from the rib and femur. It is well known that both diseases show a leucopenia and decrease in eosinophile cells in the circulating blood (Christophers and Bentley). Perhaps the explanation for this may be that the blood destruction stimulates the marrow to activity and all its elements are included in this reaction, but the red cells are hurried away to replace the destroyed corpuscles. The eosinophile cells which do not appear in the blood may be retained in the marrow because of some chemical stimulus which repels these specialized cells, and attracts the large mononuclear cells.

" The liver may be of normal size, but is usually slightly enlarged (weight 1,600 to 2,350 grams). The colour in blackwater fever is usually a pale chestnut brown or bronze colour when there is little malarial pigment. In malaria the colour may be a greenish or slaty colour depending upon the amount of jaundice and malarial pigment. The gall bladder in acute blackwater fever is quite characteristic and is distended with a dry, curdy or finely granular, dark greenish-black bile. Focal necroses are unusual in

pernicious malaria but are common and may be extensive in blackwater fever. The liver capillaries may contain hyaline thrombi in both diseases. Hæmosiderin is found in the liver cells frequently in blackwater fever and is more conspicuous in the centres of the lobules, but it may be found in pernicious malaria. The bile canaliculi are more conspicuous in blackwater fever depending upon the depth of the jaundice.

"The brain in blackwater fever is very pale and waxy looking, but otherwise normal. In malaria the brain cortex may have a distinctive appearance, either a deep rose pink or a pale slaty colour. Its consistence is like firm jelly, and it cuts like gelatin. This firmness may be due to the great engorgement of its capillaries which are stuffed with malarial parasites and red blood cells. Ecchymoses are not rare and are present in both white and gray matter.

"The other viscera present no features of especial interest.

"This comparison of the two diseases shows a great similarity and indicates that a malarial infection is an unfailing factor in all cases. The microscopical pictures are very like and show that there is a circulating poison in both diseases which is very similar in its action, but more intense in blackwater fever. Perhaps it may be safe to state that blackwater fever is malaria plus an unknown factor—probably a poison that develops as a result of some reaction against the malaria."

W. Y.

Chatrieux (H.). Action manifeste du froid dans la fièvre bilieuse hémoglobinurique. [**Evident Action of Cold in Blackwater Fever.**]—*Bull. Soc. Path. Exot.* 1926. Jan. 13. Vol. 19. No. 1. pp. 69–71.

An account is given of three cases in which an attack of blackwater fever was precipitated by cold. These three cases are, in the author's opinion, worthy of record in that they show that blackwater can occur in persons who have been only a comparatively short time in the tropics—Case 1 had lived in Dakar for only six months—and that it may occur in people who have never previously exhibited signs of malaria. No mention is made that any of the three cases had quinine before the attack of blackwater. Reference is made to the fact that Le Dantec had observed that cold is liable to precipitate blackwater.

W. Y.

Ross (G. R.) & Peall (G. H.). **Icterus without Haemoglobinuria after Quinine Treatment.**—*Brit. Med. Jl.* 1927. Jan. 8. pp. 53–54 [13 refs.]

Reference is made to the theory of Plehn (1920) that in blackwater fever haemolysis takes place in the renal tubules and to that of Barratt and Yorke (1909) and others, that it occurs in the blood stream. [This important question has been dealt with by the reviewer in some detail; see this *Bulletin*, Vol. 19, p. 631]. It is stated that while direct proof of haemoglobinaemia may be lacking, it is possible to obtain information indirectly supporting this hypothesis from the discovery of an increased content in the blood stream of substances which are known to be derivatives of haemoglobin.

It is now generally accepted that haemoglobin is broken down in the cells of the reticulo-endothelial system, particularly, if not wholly, by the Kupffer cells which are found in the liver sinuses, and is converted into bilirubin and haemosiderin. Thus in conditions in which

haemolysis exists an increased output of bilirubin can be anticipated. Van den Bergh's test not only affords a measurement of the amount of bilirubin present, but it also distinguishes between what might be termed mature and immature bilirubin in the serum. Mature bilirubin is that which has passed through the polygonal cells of the liver, and has then been absorbed into the blood stream, and is present in cases of obstructive jaundice; this variety gives the direct reaction. If, however, owing to rapid blood destruction, bilirubin is produced at so rapid a rate that the polygonal cells are unable to deal with it *in toto*, the excess is absorbed directly into the blood stream from the Kupffer cells, and forms the immature bilirubin which gives the indirect reaction. Such a reaction can be accepted as evidence of intravascular haemolysis.

In haemoglobinuric fever, in the initial stages of the disease, the indirect reaction is strongly positive and the number of units of bilirubin shows a huge increase in the normal amount of ·2 to ·5 units found in normal controls. There is thus indirect evidence that the haemoglobinuria in blackwater fever is accompanied by haemoglobinaemia. Two mechanisms at least come into play in the endeavour to rid the body of the haemoglobin dissolved in the plasma. First there is an increase in the activity of the reticulo-endothelial system, so that as much as possible of the haemoglobin may be disposed of by the normal methods of converting it into bilirubin. This we know does happen. If, however, the amount of haemoglobin is in excess of the maximum with which the reticulo-endothelial system can deal, then excretion by the kidneys occurs, with consequent haemoglobinuria. It cannot be assumed at present that the reticulo-endothelial system functions equally in every individual, but it is known that if the haemolysis be slow and gradual, as in pernicious anaemia, or even sudden but relatively slight, as in malaria, haemoglobin does not appear in the urine.

Turning to the question of quinine haemolysis *in vivo*, the author writes that it is conceivable that if quinine can produce haemolysis sufficient to cause haemoglobinuria, cases might occur in which the degree of haemolysis is so slight that the free haemoglobin can be disposed of entirely by the reticulo-endothelial system without the appearance of haemoglobin. Koch (1898) stated that after the administration of quinine an attack of icterus may occur; and Blacklock (1923) believes that haemolysis with slight jaundice can occur without haemoglobinuria and that this condition is frequently due to the same cause as blackwater fever. [See this *Bulletin*, Vol. 21, p. 62.]

Details are then given of a case which can be regarded as an example of haemolytic jaundice after quinine treatment without the development of haemoglobinuria. This case in the author's opinion is an example of an intravascular haemolysis, evidenced by jaundice, but with no accompanying haemoglobinuria. It is noted that the icterus did not make its appearance clinically until the twelfth day after commencement of the quinine treatment, but the sallowness of the patient and lemon-yellow conjunctivae, so characteristic of chronic malaria, prevented the appreciation of slight additional degrees of icterus. Furthermore, the dosage of quinine was exceedingly small; only $1\frac{1}{2}$ grains were given daily and only $5\frac{11}{32}$ grains had been given altogether when the jaundice became clinically apparent. The disappearance of the icterus on the stoppage of quinine treatment affords additional support to the belief that the quinine acted as a haemolytic agent

W. Y.

Baker (S. L.) & Dodds (E. C.). **Obstruction of the Renal Tubules during the Excretion of Haemoglobin.** – *Brit. Jl. Experim. Path.* 1925. Oct. Vol. 6. No. 5. pp. 247–260. With 3 text figs. & 1 plate. [2 refs.]

The authors refer to the work of Yorke and Nauss (1911), who showed that it was possible to produce in some cases a renal obstruction in rabbits by injecting them with solutions of their own haemoglobin; this was due to the fact that the pigment, as it passed through the kidneys, became precipitated in the tubules and so produced an obstruction.

The authors' own investigations concern intra-renal obstruction as observed on two occasions during the last two years in patients who have succumbed from renal insufficiency following blood transfusion, and an experimental investigation into the mechanism of production of renal lesions during the excretion of haemoglobin. Clinical details are given of the pathological appearances of the kidneys. The renal lesions appeared to be identical with those known to occur in blackwater fever. Turning to their experimental work, the authors confirm the observations of Yorke (1911) and of Baylis (1920) that rabbits injected with haemoglobin are liable to die suddenly either during, or shortly after, the injection. They found, however, that if the haemoglobin solutions were efficiently filtered, sudden death was avoided. The effect of the injections on the renal functions was controlled by the animal's blood urea. Several injections (10–15 cc. each) of strong haemoglobin solution produced gradually rising blood urea. After seven such injections spread over a period of three weeks, the animal was in a very weak state with a blood urea of 297 mgm. per 100 cc. The conditions of the kidneys resembled that described by Yorke and Nauss. It was observed that the brown urine showing a granular precipitate was always strongly acid, while the red urine was neutral or alkaline. As Yorke and Nauss have noted, it is impossible to produce renal obstruction in rabbits, unless the animals are kept short of green food. The correlation between acidity of the urine and the brown granular casts which obviously tend to obstruct the renal tubules lead the authors to consider the influence of diet on the reaction of the rabbit's urine. Rabbits normally pass strongly alkaline urine, but in the absence of green food, although unlimited water is supplied, the urine can be kept permanently acid.

An experiment is described in which the rabbit was fed for several days on a diet of oats and bread with unlimited water; its urine quickly became acid: another rabbit was fed on an ordinary diet containing plenty of green food, and passed strongly alkaline urine. Each was given about 10 cc. of a strong haemoglobin solution. The first rabbit passed the haemoglobin out as a brown precipitate suspended in an acid urine containing numerous brown granular casts, and its blood urea rose to 78 mgm. per 100 cc.; the second passed red alkaline urine containing abundant oxyhaemoglobin and no brown precipitate or casts, and its blood urea remained normal, i.e., 35 mgm. per 100 cc. Later experiments showed that not only increased acidity but increased salt concentration was concerned in the precipitation of haemoglobin, but high salt concentration without the required degree of acidity produced no precipitation of the haemoglobin. Further experiments showed that a return to a diet containing green food aids in the recovery of renal function after temporary blockage of the tubules caused by haemoglobin injections.

Spectroscopic examination proved that the brown pigment in acid urines was mainly methaemoglobin and that in the red specimens of alkaline urine the bands of oxyhaemoglobin predominated. The paper closes with a discussion on the relation between the hydrogen ion concentration of the medium and the nature of the pigment formed.

The following summary is given :—

"1. Two cases of intra-renal obstruction caused through blood transfusion are described and compared with the intra-renal obstruction of blackwater fever.

"2. A method for the preparation of strong haemoglobin solutions suitable for injecting into rabbits is described.

"3. The urine passed by rabbits after injection of haemoglobin is found to be either (*a*) red, alkaline in reaction and showing the bands of oxyhaemoglobin ; or (*b*) brown, acid in reaction, with a brownish deposit in the form of granular casts and amorphous *débris*.

"4. Rabbits on an ordinary diet and passing an alkaline urine are unaffected by haemoglobin injections, but if the urine is kept acid by means of a suitable diet an intra-renal obstruction can be produced.

"5. A series of *in vitro* experiments prove that haemoglobin is thrown out of solution when (*a*) the reaction of the medium is not more than about pH 6, and (*b*) the NaCl content is about 1 per cent. or over.

"6. From these experiments it would appear that haemoglobin is excreted in solution in the glomerular transudate. After concentration in the tubules the acidity and the salt concentration increase, with the result that the pigment is precipitated, probably in the form of haematin.

"7. This theory would explain the production of intra-renal obstruction in cases of the type described and in blackwater fever.

"8. A suggestion for the treatment of these conditions, based on the above conclusions, is offered, namely, the production of alkaline diuresis."

W. Y.

Asbelew (W. N.). Zur Frage des Zusammenwirkens lipoider Substanzen mit Chinin und ihrer hämatoxischen Wirkung in Verbindung zur Hämoglobinuriepathogenese. [**On the Question of the Combined Action of Lipoid Substances and Quinine, and their Haemotoxic Action in Combination, in the Pathogenesis of Haemoglobinuria.**] —*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1926. Apr. 8. Vol. 47. No. 1. pp. 89–96. [4 refs.]

The following summary is given :—

1. Lipoid substances cannot activate the haemolytic action of quinine *in vivo*. Lecithin influences quinine haemolysis *in vitro* only so far as it is itself haemolytic and acts on serum free corpuscles.

2. In the blood serum no substances have so far been demonstrated which can serve as activators in quinine haemolysis. The observations on this subject made by Kritschewsky *in vitro* with quinine concentration of ·25 to ·4 per cent. are probably to be attributed to physical changes in the medium following the action of the quinine on the serum protein.

3. The view that haemoglobinuria in malaria is a combined action of quinine with the lipoid substances of the organism, finds no support from the author's *in vitro* experiments.

4. The blood serum in the acute stages of malaria has in the majority of cases an antihaemolytic power.

5. Quinine treatment is no contraindication for the intravenous lecithin treatment.

W. Y.

Le Dantec (A.). Note sur un cas d'accès bilieux hémoglobinurique accompagné de syndrome de Raynaud. [**Haemoglobinuria accompanied by Raynaud's Syndrome.**]—*Bull. Soc. Path. Exot.* 1926. Oct. 13. Vol. 19. No. 8. pp. 680–686.

Details are given of a patient, aged 31, who on his tenth voyage to West Africa, had two attacks of bilious haemoglobinuria accompanied by the syndrome of Raynaud. The patient had never taken prophylactic quinine, and on the previous voyage had suffered from two attacks of tropical malaria. On January 17th, 1926, he noticed that his fingers had suddenly become benumbed, and consequently went to the ship's surgeon, who found albuminuria and ordered rest and two doses of ·25 gm. of quinine daily. The next day the urine was black, but there was no fever, and the fingers were gradually losing their numbness. The quinine was continued and the symptoms subsided, so that by January 21st the urine was clear and the fingers normal. On February 26th, i.e., 40 days after the first attack, he again experienced numbness of the fingers and was excused his work ; at mid-day, without having had any drug, the urine was found to be black. No drug was given —the patient simply resting and taking milk diet—and on March 1st, when the vessel arrived at Bordeaux, the patient came under the care of the author. The fingers and ears were pale and cold whilst the palms and soles were of normal temperature ; the urine was black, there was bilious vomiting, the conjunctivae were slightly icteric, the radial pulse was small and frequent, the expression was anxious, and the temperature was normal. The liver and spleen were slightly enlarged. Calcium chloride and hot drinks were given, and hot water bottles were applied to the feet ; the symptoms gradually disappeared, and the next day the urine was normal.

Examination of the blood was negative, neither malaria parasites nor spirochaetes being found ; the leucocyte formula was normal ; the Wassermann reaction performed on five occasions was always positive and remained so even after a course of arsenobenzol. Inoculation of 10 cc. of the blood into a guineapig was without result. The patient denied venereal disease, and medical examination failed to reveal any evidence of syphilis, acquired or hereditary.

The interesting observation was made that the blood of the patient laked in a pipette, previous cooling of the finger or shed blood being unnecessary to provoke the phenomenon. This red cell fragility persisted for 2 or 3 months after the attack and then gradually disappeared.

W. Y.

Repetto (R.). Sur le traitement de l'hémoglobinurie. [**Treatment of Haemoglobinuria.**]—*Ann. Soc. Belge de Méd. Trop.* 1926. July. Vol. 6. No. 2. pp. 161–164.

The author states that on his arrival in the Congo in 1910, he was given very contradictory advice on the question of the desirability of giving quinine in cases of blackwater fever. The first three cases of the disease which came under his care at Lokandu he treated with subcutaneous injections of normal saline without any quinine ; all recovered. Encouraged by these results he treated successfully three other very severe cases at Lisala. Later, at Boma, he treated six patients with intravenous injections of phosphated physiological saline, one of whom died.

From 1921 to 1923, he treated six cases with collobiase of arsenic and quinine, given intravenously, according to the method of Letuile-Roux, combining this in the severe cases with the intravenous injections of phosphated physiological saline ; all these cases recovered.

The author contrasts these results with those of ZERBINI at Katanga, who treated his cases with injections of quinine in doses of 1 to 1·5 grains (of the 28 cases so treated six died) ; and concludes [in the reviewer's opinion without any justification] that there is some peculiar virtue in the collobiase of arsenic and quinine.

W. Y.

TARDIF. Cinq observations de fièvre bilieuse hémoglobinurique traitée par la méthode de Boyé (sérum antivenimeux). Note du Médecin Inspecteur Boyé. [**Five Cases of Blackwater Fever treated by Antivenomous Serum.**]—*Ann. Méd. et Pharm. Colon.* 1926. Apr. May-June. Vol. 24. No. 2. pp. 219–226.

Blackwater fever is not common in Gabon and is met with particularly in the so-called dry season, which lasts from May till October, when the temperature is relatively low. Details are given of five cases treated by the method of Boyé with antivenom serum. All recovered, but four of them suffered from relapses about the seventh day.

W. Y.

BURKITT (R. W.). **Treatment of Blackwater Fever.**— *Kenya Med. Jl.* 1926. June. Vol. 3. No. 3. pp. 89–90.

The author states that there are two outstanding things to be done in the treatment of blackwater fever :—

" 1. Do away with the product of malaria saturation, viz. acidosis. Where this is done thoroughly the haemoglobinuria ceases.

" 2. Do away with the primary cause, viz. malaria."

He states that when possible sodium bicarbonate should always be given intramuscularly, and that when this is done, the haemoglobinuria will soon cease. He further considers that the tincture of cinchona bark might, with advantage, be given at first instead of quinine, and will be less likely to produce a relapse of blackwater.

W. Y.

HANSCHELL (H. M.). **Intravenous Alkaline Infusion in Blackwater Fever.** —*Trans. Roy. Soc. Trop. Med. & Hyg.* 1926. Feb. 18. Vol. 19. No. 8. pp. 488–491. [2 refs.]

This paper records a case of blackwater fever treated successfully by intravenous administration of sodium bicarbonate. The author writes :—

" Modesty, and caution bred of some knowledge of this disease would usually prevent one such case being thought worthy of record ; and, most of all, any claim for the specific efficacy of a drug used in one case only. Indeed, but for some recent work of Baker and Dodds (October, 1925), the writer was resigned to the thought that he had put in an ineffectual attendance on yet another sick human being, doomed from the start to recovery."

Details of the case are briefly as follows :—

European male, aged 47 years, had recently returned from West Africa, where he had had many attacks of fever, notwithstanding the fact (so he stated) that he had taken 5 grains of quinine daily. The author treated him for syphilis over a period of nine months, and half way through this course the patient developed fever, *P. falciparum* being found in the blood. Three months after cessation of anti-syphilitic treatment the author was called in to see the patient in his lodgings. He had then been ill for 2½ days without medical attention ; he had diagnosed his own case as blackwater fever, and had remained in bed and treated himself by frequent liberal draughts of beer. On examination he was found to have deep jaundice, an anxious face, pulsating neck, large liver and spleen, small rapid pulse, indistinct heart sounds, and haemic murmurs. The temperature was 103·4° F. Vomiting had begun eight hours previously and was now frequent. No urine had been voided for over five hours, the whole of the last specimen measured just over one fluid ounce, which was almost black with a heavy brown granular deposit. The patient complained of severe headache and lumbar pain and had fainted on sitting up in bed about two hours before the author arrived. Two hours later the patient was unable to talk or move, the vomiting had ceased, the temperature was 104·4° F. and no urine had been passed ; a catheter drew off about half an ounce of black urine with a heavy granular deposit consisting of granular and cellular casts, epithelium cells, a few leucocytes and red cells and much yellowish granular débris.

The patient was given intravenously 20 fluid ounces of distilled water in which had been dissolved 150 grains of sodium bicarbonate. Noticeable improvement in the pulse followed and the injection was repeated one hour later. About fifteen minutes after the second injecoisn the catheter drew off about four ounces of urine less black and with less deposit, and the patient's general condition had unmistakably improved. Yet an hour later, the catheter drew off some 12 ounces of translucent red urine with a little deposit, and the patient, after a few moments of shallow sighing, yawned and fell asleep. Diuresis with progressively clear urine continued and convalescence followed rapidly.

W. Y.

Braimbridge (C. V.). **Decapsulisation of the Kidney in Blackwater Fever.**—*Kenya Med. Jl.* 1926. Dec. Vol. 3. No. 9. p. 267.

Decapsulization of both kidneys was performed in a patient with blackwater fever who had exhibited complete suppression of urine for three days. There was a certain amount of urinary secretion during the following 24 hours, but suppression returned and the patient eventually died.

W. Y.

Twells (T. W.). **A Case of Blackwater Fever.**—*Indian Med. Gaz.* 1927. May. Vol. 62. No. 5. p. 268. With 1 chart.

Details are given of a case of blackwater fever, in a European aged 25 who had lived for more than six years in India and previously had never had malaria and had never taken quinine. When first seen by the author the patient was passing blackwater and his blood contained *P. falciparum.*

Three days later, as parasites were still present, quinine, grains 2, were given daily and the dose was gradually increased to 20 grains daily. The patient made an uninterrupted recovery.

W. Y.

Cardamatis (Jean P.). La fièvre bilieuse hémoglobinurique observée en Grèce. **Blackwater Fever in Greece.**] —*Grèce Méd.* 1926. Mar.-Apr. Vol. 28. No. 3–4. pp. 9–14. [21 refs.]

This article consists of a general account of blackwater fever and requires no special notice.

Weitzman (T.). **Note of a Case of Blackwater Fever in a Native of Palestine.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1926. Nov. 25. Vol. 20. No. 4. p. 274.

This note contains a brief description of a case of blackwater fever occurring in a Bedouin near Chedera, Palestine. The author considers it of some interest in view of the fact that it is generally accepted in Palestine that blackwater fever does not occur in natives.

Wallington (K. T. K.). **Two Cases of Blackwater Fever occurring within Ten Days at Broderick Falls, Uganda Extension Railway Construction.**—*Kenya Med. Jl.* 1927. Mar. Vol. 3. No. 12. pp. 357–359.

Clinical details are given of two cases of blackwater fever, one followed by death and the other by recovery.

Anderson (James S.). **Blackwater Fever in Scotland.**—*Lancet.* 1927. Jan. 1. pp. 18–19.

This is a note concerning an attack of blackwater fever in a patient who had four months previously been in West Africa.

Kritschewsky (I. L.). Zur Hämoglobinuriepathogenese bei Malaria. **The Pathogenesis of Haemoglobinuria in Malaria.**] —*Arch. f. Schiffs- u. Trop.-Hyg.* 1926. July 1. Vol. 30. No. 7. pp. 293–294. [4 refs.]

This is a rejoinder to Kessler who, so Kritschewsky complains, misquoted him when commenting on his paper on the pathogenesis of blackwater fever. (This *Bulletin*, Vol. 21, p. 386, and Vol. 23, p. 69).

Plehn (Albert). Demonstrationen und Erläuterungen zur Schwarzwasserfrage. **Demonstrations and Explanations on the Blackwater Fever Problem.**]—*Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* 1926. Vol. 30. No. 1. pp. 56–61. With 4 text figs. [1 ref.]

The matter contained in this address has already been discussed in a previous paper, which has been fully summarized and the subject of a critical review in this *Bulletin* [Vol. 17, p. 313 and Vol. 19, p. 631].

W. Y.

Cosimo (Basile Vito). A proposito di un caso di febbre biliosa-emoglobinurica. **A Case of Bilious Haemoglobinuric Fever.**] —*Ann. di Med. Nav. e Colon.* 1927. Mar.–Apr. Year 33 (Year 5). Vol. 1. No. 3–4. pp. 168–175. With 1 chart in text.

A typical case of blackwater occurring in a malarial subject after a large dose of quinine, 3 gm. of the hydrochloride "intravenously and by mouth" in 24 hours.

H. Harold Scott.

MISCELLANEOUS.

COOLEY (Thomas B.) & LEE (Pearl). **The Sickle Cell Phenomenon.**—*Amer. Jl. Dis. Children.* 1926. Sept. Vol. 32. No. 3. pp. 334–340. With 3 text figs. [4 refs.]

The observations here reported were made in the Children's Hospital of Michigan, where for ten months the blood of all the negro children admitted was examined for sickle cells, and, so far as was possible, the blood of the relatives of the affected children also. The authors confirm the statements that sickle-cell anaemia is congenital and hereditary, and believe that transmission may be through the mother. They conclude from their observations that the mere presence of sickle cells in the blood does not necessarily imply anaemia or, indeed, any deviation from the normal standard of health, although the sickle-cells disappear rapidly when the blood is incubated, and although their presence is sometimes associated with haemolytic jaundice. The authors are disposed therefore to draw a line between the two alternatives and to restrict the term " sickle-cell anaemia " to the cases where sickle cells and haemolytic jaundice are concurrent phenomena.

The following is the summary of their observations :—

" Of 400 coloured patients in the Children's Hospital, 30, or 7·5 per cent., were found to have sickle cells. Of the parents of the 30 children, 15 mothers and 6 fathers were examined ; 11 mothers and 1 father showed sickle cells, and in this one case the mother also showed them. With two exceptions, none of the children showed an anemia differing in any way from the average of a corresponding number of children without sickle cells. There was no history of anemic symptoms, nor of jaundice, in the children or their families, and no signs or history of leg ulcers ; nor can we find that leg ulcers of the type described occur in the coloured population at large. Yellow sclerae are not observed. Roentgenograms show nothing characteristic in the skull and long bones. Necropsies on three out of four children who died gave no significant findings. Two children have shown a mild grade of hemolytic jaundice. They had greenish-yellow sclerae, pigmented blood serum, positive indirect van den Bergh reaction, and increased urobilin. Gastric hydrochloric acid was diminished in one, and absent in the other. There were leukocytosis and moderate anemia with normoblasts, polychromatophilia and reticulation. The spleens were not enlarged, and no gland swellings were noted. There were no ulcers nor scars. Roentgenograms of the skull and long bones in one gave slight indication of changes like those we have noted in another form of chronic hemolytic anemia. Clinically, these two cases have nothing to suggest a separate disease entity.

" Our studies of the phenomena of sickling confirm, in general, those of other observers. We have two new facts to add : (1) In preparations kept at incubator temperature, the sickle cells disappear rapidly from the blood, leaving the round cells behind ; (2) the cells of one of the patients with hemolytic anemia are rapidly hemolyzed at incubator temperature in their own serums and in serums from normal bloods, while the serum of this patient is not hemolytic for normal cells. This test has not yet been applied to any number of sickle cell bloods. These two observations seem to imply a special vulnerability of the sickle cell."

The authors commend the subject, and particularly its congenital (and possibly tribal) aspects to the attention of medical men in Africa.

A. A.

Lee (Douglas H. K.). **Blood Groups of North Queensland Aborigines, with a Statistical Collection of some Published Figures for Various Races.**—*Med. Jl. Australia.* 1926. Sept. 25. 13th Year. Vol. 2. No. 13. pp. 401–410. With 3 figs. [22 refs.]

This important paper is the outcome of a survey of 377 Australian aborigines of Palm Island Settlement, about 40 miles N.N.E. of Townsville (Queensland). In the first part of the paper the author describes his methods and technique and his results; in the second part he discusses, on a wealth of statistical detail, the geographical variation of the racial or biochemical index.

The author's 377 aborigines were, to all possible assurance, pure stock. Their bloods were sorted, according to the method of Moss, as follows: Group I, 60·3 per cent.; Group II, 31·7 per cent.; Group III, 6·4 per cent.; Group IV, 1·6 per cent.; giving a biochemical race-index of 4·2. This determination does not actually coincide with the determinations of other authors in other Australian areas, but it agrees with them in being high in the world series.

Dealing with the geographical undulation of the biochemical race-index the author remarks upon the existence of certain gaps in the statistical requirements, namely, for South American natives, Maoris, Fijians, South African Bushmen, Norwegians, Swedes, and Eskimos. Taking the data as they exist at present the author uses them graphically. From his map "it will be seen that India forms the centre of a cone-like depression with an index of 0·56 and that as we pass out from it the figures for the most part show a steady gradient, but more especially to the east and west, until the extremes of 5·35 in north-west Europe and 5·7 in Australia and 9·2 in North America are reached." The author thinks that the explanation of this geographical conformation is not to be found in racial adaptations to "geographical" factors, but may perhaps be sought in connexion with the place of origin and subsequent migrations of Man.

A. A.

Proescher (Frederic) & Arkush (Albert S.). **Acetone Methylene Blue –Methylene Azur Eosin Solution for Staining Blood Smears.**—*Jl. Lab. & Clin. Med.* 1926. Apr. Vol. 11. No. 7. pp. 682–683.

The following stain is said to be very similar in effect, while comparing "very favourably," with the commonly used eosine-methylene-blue stains.

Equal parts (about 60 mgm. each) of methylene blue (Merk), thiazin red (methylene azur), and eosin are mixed with 25 cc. of water, and 50 cc. of acetone then added. The acetone should be C.P. (Toluidin blue may be used instead of methylene blue. Grübler's eosin (extra BA) is much preferable to the domestic eosin). By substituting orange G for part (about one third) of the eosin, eosinophile granules become slightly more prominent. The proper intervals for the stain should be determined by trial each time it is made up, and care then taken that the acetone does not evaporate. The advantages of this stain are said to be its rapidity, easy preparation and economy, and its not requiring a buffer for dilution or washing.

A. A.

Suldey (E. W.). Méthode de coloration rapide pour recherches hématologiques. **Rapid Blood Stain.** *Bull. Soc. Path. Exot.* 1926. Oct. 13. Vol. 19. No. 8. pp. 723–724.

The technique is as follows :—

(1) Prepare—1 per cent. toluidine blue 10 ; neutral distilled water 40 ; 95 per cent. alcohol 10 to 15. (2) Use dry films, unfixed. (3) Stain. (4) Drain. (5) Repeat the staining. (6) Dry gently with paper. (7) Examine without coverglass under an oil immersion lens, applying the cedar oil to the film just as the moisture is disappearing.

Metachromasia, endo- and extra-corpuscular parasites are well brought out.

W. F. H.

Morgan (Julia). **Notes on Stovarsol Poisoning.** *China Med. Jl.* 1926. Nov. Vol. 40. No. 11. pp. 1086–1090. [14 refs.]

The author notes that stovarsol (acetyl aminophenyl-arsenic acid) contains 27 per cent. arsenic and is as a rule well tolerated. The majority of writers recommend an adult dose of 0·5 to 1·0 gm. daily for a week or more, with repetition if necessary after a few days. The practice of a number of authors is described. A few cases of poisoning have been reported, with one exception extremely mild. The author records three cases of poisoning, two severe and one mild, among eight patients treated at Tsinanfu. The dosage followed was as above, 0·25 gm. being given thrice daily, but after 2 cases of poisoning had occurred the frequency was reduced to twice ; the most severe symptoms appeared after administration of 2·0 gm. Full details are given. The cases were dysentery, amoebic in two instances. In each case fever (up to 105°) was the first symptom, followed two days later by rash and bronchitis. The rash appeared all over the body, or spared the legs and face, and is described as "a diffuse roseolar macular dermatitis," and in the other cases as "morbilliform" and "reddish maculo-papular." Sodium thiosulphate was given in two instances. It is suggested that careful temperature records should be kept and the administration suspended if the temperature rises.

In discussion D. Meleny said there had been three cases of stovarsol poisoning at Peking, one fatal.

A. G. B.

Napier (L. Everard). **Reactions following the Administration of the Pentavalent Compounds of Antimony : an Analysis of Cases reported by Several Correspondents.**—*Indian Med. Gaz.* 1926. Nov. Vol. 61. No. 11. pp. 559–561.

In the course of a year the author at Calcutta has received reports on reactions following the administration of pentavalent compounds of antimony in 13 cases ; he gives brief details of each. In 8 urea-stibamine (Brahmachari) was the compound used, in 3 stiburea (Union Drug Co.) and in 2 amino-stiburea ; the symptoms could not be grouped according to the compound used. In most cases they appeared after one of the later injections, from the 6th to the 17th. In most cases again it was the maximum dose that caused the first symptoms, but

the maximum dose had usually been administered already without such an event. The symptoms appeared very shortly after the injection and usually in the following order :—

"The patient had a burning sensation all over the body ; the eyes became puffy and there was swelling of the face ; an urticarial rash appeared on the face and all over the body ; there was a sensation of suffocation, apparently caused by oedema of the mucous membrane of the throat, which was in some instances followed by loss of voice and in others by severe dyspnoea ; in a few instances there was a marked rise of temperature and pulse rate, but in the most severe cases there was collapse and vomiting ; and in one instance the patient passed into a semi-conscious state."

"The symptoms usually disappeared rapidly, but in a few the swelling of the face persisted for 24 hours."

In two cases a severe shivering attack lasting for about 2 hours was the main phenomenon.

The author discusses the symptoms and finds they suggest anaphylaxis with sensitization by the previous injections. They were not due to overdose nor to antimony poisoning. In none was the issue fatal, and no one need hesitate about using these preparations. "The great decrease in the death rate amongst treated cases [kala azar] that has been effected since the pentavalent compounds were introduced is an irrefutable argument in favour of adopting these in the place of sodium antimony tartrate whenever possible."

The attack may be cut short by adrenalin and recovery accelerated by strychnine and digitalin. Great caution should be used in the subsequent injections, which should not amount to more than one tenth of that which caused the symptoms.

A. G. B.

CARMAN (J. A.). **A Case of Idiosyncrasy for Carbon Tetrachloride.**—*Kenya Med. Jl.* 1926. Dec. Vol. 3. No. 9. pp. 260–261.

Seventy boys were treated for hookworm in batches of 10 with carbon tetrachloride and magnesium sulphate. The first batch received 2 cc. of CCl_4, and the next five batches 3 cc. [33 cc. in text] with no signs of poisoning. The last batch had 4 cc. followed immediately by magnesium sulphate. One of these boys half an hour later complained of a sensation of giddiness and within two minutes lay down and became incapable of speech, with shallow respiration and thready pulse ; unconsciousness rapidly followed. Whisky and strychnine were administered without effect and the breathing stopped. Artificial respiration was commenced and continued for 10 minutes, when the patient sat up. "His behaviour was that of a patient recovering from an anaesthetic." The next day he complained of pain over the liver and was unsteady on his feet. The purgative had acted, it is stated, before the onset of symptoms.

The conclusions drawn are that 3 cc. is the largest safe dose of the drug, that if symptoms of poisoning appear deep breathing should be commenced or, if the patient is unconscious, artificial respiration, and that ether, for its effect on the respiratory centre, would be the best stimulant to administer hypodermically.

A. G. B.

Lamson (Paul D.) & Wing (Raymond). **Blood Fibrin and Levulose Tolerance in Acute and Chronic Carbon Tetrachloride Intoxication.** —*Jl. Pharm. & Experim. Therap.* 1926. Sept. Vol. 28. No. 3. pp. 399–408. With 2 text figs. [11 refs.]

The following are the conclusions of this paper; the subjects were dogs:—

"1. A certain threshold dose of carbon tetrachloride by mouth, approximately 0·25 cc. per kilo, is necessary to produce a fall in blood fibrin. Larger doses (up to 6 cc. per kilo) cause no greater fall.

"2. Maximum oral doses of alcohol alone produce no change in blood fibrin.

"3. The simultaneous administration of alcohol and carbon tetrachloride does not reduce the threshold dose necessary to produce a fall in blood fibrin.

"4. Carbon tetrachloride administered orally in a single dose reduces levulose tolerance, the maximum disturbance occurring about three days after administration and normal tolerance being re-established in five or six days.

"5. A single dose of carbon tetrachloride produces in forty-eight hours a striking derangement of certain liver functions as shown by an increase in bile pigments in the blood, a reduced tolerance to levulose, a drop in the blood fibrin, and a disturbance of the phenoltetrachlorphthalein liver function test. Dogs chronically poisoned with large doses (10 to 25 cc.) of carbon tetrachloride given every other day for a period of approximately four months and showing tremendous liver lesions of necrosis, scar tissue formation, and all the signs of an early cirrhosis of the liver, *give normal values for all of these liver function tests.* It has been found that under the continued administration of carbon tetrachloride the blood fibrin returns to normal in two weeks in spite of the very active liver lesions found.

"6. Specific threshold oral doses of carbon tetrachloride are necessary to produce a change in the different liver functions examined. These threshold doses for the different functions are approximately 0·25 cc. per kilo to cause a decrease in blood fibrin, 0·5 to 1·0 cc. per kilo to cause pathological change, and 4·0 cc. per kilo to cause a retention of the dye, phenoltetrachlorphthalein. Larger doses than this cause no greater disturbance in function in the case of pathological change and blood fibrin. The other functions are being examined for this "all-or-none" property."

A. G. B.

i. Loevenhart (A. S.) & Stratman-Thomas (W. K.). **On the Chemotherapy of Neurosyphilis and Trypanosomiasis.**—*Jl. Pharm. & Experim. Therap.* 1926. Oct. Vol. 29. No. 1. pp. 69–82. [40 refs.]

ii. Fourneau (E.), Tréfouël, M. & Mme., & de Lestrange-Trévise. Les dérivés de l'acide phénylarsinique (arsenic pentavalent) dans le traitement des trypanosomiases. Relation entre l'action thérapeutique des acides arsiniques aromatiques et leur constitution. (Deuxième mémoire.) [**Derivatives of Phenylarsinic Acid in the Treatment of Trypanosomiasis. The Therapeutic Action of Aromatic Arsinic Acids in relation to their Constitution.**]—*Ann. Inst. Pasteur.* 1926. Nov. Vol. 40. No. 11. pp. 933–951. [14 refs.]

i. After a comparative study of twelve arsenical drugs the authors conclude that tryparsamide is the only drug of the series which can be regarded as effective in neurosyphilis. Examination of the chemical

structure of these twelve drugs leads them to the conclusion that the therapeutic effect peculiar to tryparsamide, $(HO)_2$:AsO.C_6H_4.$NH.CH_2.CO.NH_2$, is associated with the structure to the left of the .CO. group and in this structure the methylene group (.CH_2) is regarded as important. The conversion of tryparsamide into the corresponding acid (.$CO.NH_2COOH$) or ethyl ester (.$CO.NH_2CO.OC_2H_5$) destroys the activity, whilst transformation into the related primary alcohol (.$CO.NH_2CH_2OH$) gives a substance "etharsanol," which is an effective trypanocide and spirochaeticide in man and animals, but is devoid of the action of tryparsamide in neurosyphilis. The authors suggest that the value of drugs in late trypanosomiasis in rabbits, after apparent involvement of the central nervous system, is no criterion of their value in neurosyphilis.

Apart from the foregoing, which narrows but does not solve the main question, it is shown that there is no significant difference in the amounts of arsenic secreted by the gray and white matter of the brain when tryparsamide and neosalvarsan are injected intravenously, so that the suggestion made by Brown and Pearce (this *Bulletin*, Vol. 21, p. 378) that the action of the former drug in neurosyphilis is due to its greater penetrating power is untenable. The authors are therefore driven to the conclusion that the action of tryparsamide in neurosyphilis is mainly indirect and that when it is ineffective deterioration in the cells concerned must have proceeded so far that they no longer respond to stimulation by the drug.

ii. This is a further contribution to the study of the effect on trypanocidal action of the substitution of various radicals for hydrogen atoms in the nucleus of phenylarsinic acids (compare this *Bulletin*, Vol. 21, p. 322).

The chemistry of each of the compounds dealt with is described briefly, full details being reserved for publication elsewhere, and for each the tolerated and curative doses are given. The following paragraphs summarize the general results of the various substitutions as they affect the chemotherapeutic index. The insertion of a methyl group in disubstituted phenylarsinic acids has an unfavourable effect, except in the case of 3 : 4-diaminophenylarsinic acid where the 6-methyl-derivative has a definite trypanocidal effect, that of the parent substance being irregular and indeterminate. Introduction of a chlorine atom generally raises the toxicity and slightly lowers the curative dose but in general the index remains below that of the non-chlorinated product. The exceptions are 3-amino-6-chlorophenylarsinic acid and the 2-chloro derivative of tryparsamide, where the index (T/C) is raised from 0 to 1, and 3 to 5 respectively.

In the aminophenylarsinic acids neutralization of the amino-group by acylation, in general augments the index, when the amino-group is in the *para*-position to the arsenic radical. Further the acylamino-compounds are more active when given by the mouth than when injected subcutaneously, at least in mice infected with "nagana." Conversion of the amino-group into an acylamino- or a urethane group in the case of 3-amino-4-hydroxyphenylarsinic acid destroys all trypanocidal action, but its neutralization by a dimethylaminoacetyl group as in $(HO)_2$:AsO.$C_6H_2OH.NH.CO.CH_2.N(CH_3)_2$ only lowers the index T.C from 5 to 2. While 2:4-dihydroxyphenylarsinic acid has an index of 2·5, the 5-amino- derivative is devoid of action, showing that the amino- group, *per se*, has no specific influence. The whole series emphasizes the importance of the amino-group in the 4 or *para*-

position to the arsenic radical ; thus tryparsamide and its two isomerides with the glycineamide group in the ortho and *meta*- positions respectively have indexes (T/C) 3, 0, and 1. The nine possible position isomerides of 3-amino-4-hydroxyphenylarsinic acid (the parent substance of the drugs variously known as stovarsol, spirocide, acetylarsan, etc.) have now all been prepared : the only other promising member of the group is 4-amino-2-hydroxyphenylarsinic acid and this has proved to be less effective than stovarsol in the treatment of syphilis. Particular interest attaches to the influence of the acetyl residue ($CH_3.CO.$), attached to a cyclic carbon in phenylarsinic acids, since the acetophenone grouping is characteristic of "Albert 102," the precise structure of which has not been published : 4-acetophenonearsinic acid, $(HO)_2AsO.C_6H_4.CO.CH_3$, has T/C =2, i.e., it is more active than atoxyl, though it possesses neither an amino- nor a phenolic hydroxyl group.

T. A. Henry.

KÉRUZORÉ (A.). L'altération de l'atoxyl. [**Deterioration of Atoxyl.**]— *Ann. de Méd. et de Pharm. Colon.* 1926. Apr.–May–June. Vol. 24. No. 2. pp. 186–190.

A number of poisoning cases having been traced to the use of deteriorated atoxyl in the treatment of sleeping sickness, the author has devised a method of detecting such deterioration, based on the observation of FRANÇOIS that atoxyl has been known to decompose on long storage into sodium arsenate and arsenious oxide. The process depends on the detection of the former in the usual way as ammonium magnesium arsenate or as the yellow precipitate formed on addition of ammonium molybdate dissolved in sulphuric and nitric acids.

T. A. Henry.

MCCARRISON (Robert). **A Note on Lathyrism in the Gilgit Agency.** – *Indian Jl. Med. Res.* 1926. Oct. Vol. 14. No. 2. pp. 379–381. With 1 plate. [3 refs.]

The author publishes an old and interesting note dated 1908, moved thereto by the papers of ACTON & CHOPRA, and ANDERSON, HOWARD and SIMONSEN (this *Bulletin*, Vol. 20, pp. 46 and 645; Vol. 22, p. 985].

Ten cases of lathyrism developed in a village of 101 inhabitants, 5,500 feet above sea level. These were recent settlers and the soil was very unproductive. The main crop was "garash" or *Lathyrus sativus* ; the grain is ground with a small proportion of wheat (1 to 50 in one sample) and made into bread ; the villagers had lived on this for six months. Of the 10 all were males and 6 were boys. The symptoms developed after 2, 3, 4 and 5 months. The disease had reached the stage of spastic paralysis, and 7 were unable to walk without a stick. A chemical test showed that four ounces of Lathyrus seed contained an alkaloid. A feeding experiment on a monkey was inconclusive.

Colonel McCarrison draws attention to the fine physique of one of the sufferers (illustrated) indicating that the cause is a poison rather than a nutritional defect. He notes from his experience with millet seed grown under various manurial conditions that "garash" may be toxic under certain conditions of growth and not otherwise, but states that the seeds may not have been pure *L. sativus*.

A. G. B.

Iyer (A. S. Vaidyanath). **Infantile Cirrhosis of the Liver. (Its Causation and Treatment; from a Study of 59 Cases.)**—*Indian Med. Gaz.* 1926. Dec. Vol. 61. No. 12. pp. 594–596.

In a period of 4 years the author, Assistant Surgeon, Tellicherry, Madras, has treated 59 cases of infantile cirrhosis. Of these 57 were between the ages of 6 months and 3 years; the children came from both vegetarian and non-vegetarian families. In half the cases the spleen was enlarged as well as the liver. The large majority were on a mixed diet of breast-milk, cow's milk, rice and sago, and faulty digestion was believed to be the cause. Thus, a strict diet of easily digestible food soon brought amelioration, whereas the addition of rice aggravated the symptoms. The author gives goat's milk, roasted ripe bananas, fruit juices and as a rule Horlick's malted milk. All starchy foods are avoided. The administration of grey powder proved useful. Nearly half the patients recovered.

A. G. B.

Khan (Matlook). **A Cheap and Waterproof Substitute for Plaster-of-Paris in Outpost Dispensaries.**—*Indian Med. Gaz.* 1926. Nov. Vol. 61. No. 11. p. 551.

Black gram is soaked in water for 12 hours, the pericarp is rubbed away, and the white seeds are made into a paste. This is applied to one side of a soaked bandage and after each turn finely powdered building cement is rubbed in, with a final coat of paste and cement.

A. G. B.

Castellani (Aldo) & Taylor (F. E.). **Further Observations on a Mycological Method to identify Various Sugars and other Carbon Compounds.** *Jl. Trop. Med. & Hyg.* 1926. July 15. Vol. 29. No. 14. pp. 201–210. With 1 text fig. [11 refs.]

It is stated that the fermentation test for glucose by means of baker's yeast as described in many manuals of pathology and clinical methods is not specific, as usually the yeast is impure; and, even with pure cultures, levulose, galactose and saccharose may be fermented in addition to glucose. *Monilia krusei* Cast. produces acid and gas in glucose and levulose only, and for practical purpose is preferable to baker's yeast. The authors then elaborate this method for the identification of other sugars and carbon compounds, by adopting various combinations of fungi, of fungi and bacteria, or of chemical tests and fermentation tests. Numerous examples are described, and the method is regarded as being especially valuable for the identification of galactose and maltose.

P. Tate.

i. Barreto (Francisco). Contribuição ao estudo do valor diagnostico da Reacção de Gaté e Papacostas e suas aliadas. **The Diagnostic Value of the Gaté and Papacostas and Allied Reactions.** *Arquivos Indo-Portugueses de Med. e Historia Nat.* Nova-Goa. 1926. Vol. 3. pp. 49–82. [French summary pp. 83–85.]

ii. DE MELLO (Froilano). Note complémentaire sur quelques faits concernant le phénomène de formol gélification. [**Supplementary Note on the Formol-Gel Reaction.**] *Ibid.* pp. 86–98.

i. In this detailed and documented work the author has tested the value for diagnosis of (1) Gaté and Papacostas' reaction in which two drops of 40 per cent. formol are added to 1 cc. of human serum, (2) Napier's modification in which one drop of a 10 per cent. solution of phenol is added as well, (3) the first, in which the serum is inactivated at 55°, (4) Ray's globulin test, the grade of flocculation obtained when distilled water is added to serum. He employed 61 serums from normal persons, 40 from malaria patients, 30 from syphilitics, 4 tuberculosis, 6 leprosy, 6 pregnancy, and 54 from miscellaneous diseases.

The conclusions reached were :—

(1) The Gaté and Papacostas reaction does not seem to have any diagnostic value, since we have found it not only in syphilis, tuberculosis and leprosy, but also in other diseases and even in normal persons.

(2) Napier's reaction does not seem to have the high diagnostic value which its author attributed to it since the opacity has been seen in our observations in malaria, syphilis, leprosy, tuberculosis, amoebic dysentery and other diseases.

(3) Ray's reaction does not seem of diagnostic value since we have found it positive even in normal serums.

(4) Inactivation seems to hasten the phenomenon of formol gelification.

(5) Phenol seems to retard it to a certain extent.

ii. Professor Froilano de Mello has repeated the work of his pupil, BARRETO, employing 9 serums from normal persons, 5 tuberculosis, 5 syphilis, 11 malaria and 10 various skin conditions and has confirmed the work of BARRETO. He then tested the same patient on more than one occasion and afterwards a series of patients daily for a week. He found that negative reactions later became positive and that the degree of opacity increased with the quantity of formol added. He concludes that the formol-gel reaction and its modifications present such variations that they cannot be employed for the diagnosis of disease.

A. G. B.

SISON (A. G.), SISON (A. B. M.), IGNACIO (M.) & NAVARRO (R.). **Splenic Anemia among Filipinos.**—*Far Eastern Assoc. Trop. Med. Trans. Sixth Biennial Congress, Tokyo, 1925.* Vol. 2. pp. 271–275 ; also in *Jl. Philippine Islands Med. Assoc.* 1926. Oct. Vol. 6. No. 10. pp. 330–332.

The authors examined the records of all admissions to the Philippine General Hospital for a period of 13 years and also the autopsy records for the same period. Fifty admissions, or 0·2 per cent., were diagnosed clinically as splenic anaemia or Banti's disease. Of 20,000 autopsies, made during the same period, in 24 the same condition was recognized. Of the 50 cases 38 were between 20 and 40 years ; 14 suffered also from tuberculosis of the lungs and 10 from nephritis ; in 22 there was a history of malaria. A record is furnished of the intestinal parasites found in the 50. All had a large spleen, 80 per cent. had fever, 58 pallor, 56 per cent. had enlarged liver, and 46 and 40 per cent. ascites and jaundice. The blood counts showed a moderate degree of anaemia

of the secondary type with a tendency to leucopenia. An account is given of the autopsy findings. There was hepatic cirrhosis of the portal type.

A. G. B.

GLASER (R. W.). **Acquired Immunity in Silkworms.**—*Jl. of Immunology.* 1925. July. Vol. 10. No. 4. pp. 651–662. [7 refs.]

The author notices the paucity of recorded experiments on acquired immunity in insects. He discusses two different instances of acquisition of immunity to virulent bacilli by insects, the immunity being imparted by a prior inoculation, in the one instance of an old culture, in the other by a heat-killed culture, of the specific bacillus. In the latter instance as in most of the recorded experiments both on natural immunity and on acquired immunity in insects the bacillus employed was " foreign " to the insect employed in experimentation, i.e., was not one that in the ordinary course of things is the cause of a specific insect disease. The author's experiments here described were made in connexion with a specific flacherie-like disease of silkworms, and the following are his conclusions :—

" Acquired immunity towards a " Flacherie "-like disease was produced in a large number of silkworms by injecting killed cultures of the specific bacillus. Subsequent infection by feeding the living bacillus rarely produced the disease. A single treatment with vaccine so employed, perhaps, demonstrates some immunizing effect, but more than one treatment is necessary to obtain a pronounced effect.

" Acquired immunity against this disease was not produced by feeding vaccine, followed by feeding the living culture ; nor was any noticed by injecting the vaccine, followed by the inoculation of a minimum lethal dose of the living culture."

A. A.

DE MELLO (Froilano). Syndrome anaphylactique après l'injection d'un gramme de chlorydrate de quinine. **Anaphylaxis after Injection of a Gramme of Quinine Hydrochloride.**—*Bol. Ger. Med. e Farmacia.* Bastora. 1926. Jan.–Sept. Vol. 11. Nos. 1–9. pp. 28–29.

LE DANTEC in his text-book of tropical medicine states that anaphylaxis occurs only after the ingestion of quinine, never after its parenteral administration. The author relates the case of a soldier who after an injection of 1 gm. quinine hydrochloride developed general urticaria with intolerable pruritus, dilated pupils and thready pulse.

A. G. B.

BISHOP (Louis Faugere). Cardiovascular Disease in the Tropics.—*Amer. Jl. Trop. Med.* 1926. Nov. Vol. 6. No. 6. pp. 455–460.

BLONDIN. Utilisation par les indigènes de " Caisses de Secours " en dépôt dans les villages.—*Bull. Soc. Path. Exot.* 1926. Dec. 8. Vol. 19. No. 10. pp. 943–944.

COLE (H. A.). Gonococcal Abscess in the Wall of Uterus simulating an Ovarian Tumour.—*Kenya Med. Jl.* 1926. Sept. Vol. 3. No. 6. pp. 171–173.

DARGEIN (G.) & DORÉ (G.). Un cas de mort par le tréparsol.—*Bull. et Mém Soc. Méd. Hôpit. de Paris.* 1926. Dec. 2. Year 42. 3rd Ser. Vol. 50. No. 36. pp. 1653–1656.

FAUQUÉ (M. C. J.). Sur un cas de méningococcémie à type palustre avec purpura ayant abouti au bout de 41 jours à une méningite cérébro-spinale.—*Arch. Méd. et Pharm. Milit.* 1926. Sept. Vol. 85. No. 3. pp. 296–299. With 1 chart.

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REVIEWS AND NOTICES.

ANALES DE LA FACULTAD DE MEDICINA. Lima. Numero Extraordinario. 1925. Oct. 1. 106 pp. With 6 plates, 1 chart & 1 fig.

This special number of the organ of the Lima Faculty of Medicine, which is the first to be published in the nine years of its existence, has been issued to commemorate a meeting of the Faculty held on September 8th, 1924, when an honorary degree was conferred on Dr. Alberto BARTON in recognition of his valuable work on verruga peruviana and addresses were given by Dr. Telemacho BATTISTINI and Professor MONGE on the experimental inoculation of the disease.

Barely a third of this interesting issue, however, is occupied by the proceedings of the meeting, the remaining two-thirds being devoted to other papers on verruga peruviana, or Carrion's disease, as it is often called in Peru in honour of the heroic student Daniel A. CARRION, who as Dr. Carlos MONGE relates in a special memoir, successfully inoculated himself on August 27th, 1885, in both arms with blood from a verruga lesion to determine whether verruga was related to Oroya fever or a distinct clinical entity.

CARRION'S thesis on verruga, which was published posthumously in 1886, is reproduced with an account of his last illness, part of which was recorded by himself.

The remaining 40 pages consists of obituary notices of CARRION from the scientific and lay press of various countries with the appreciation of his self sacrifice. Mention should also be made of a Peruvian bibliography of Verruga compiled by Dr. Hermilio VALDIZAN.

This issue, which will appeal with equal force to those interested in tropical diseases and the history of medicine, is illustrated by portraits of CARRION, BARTON and BATTISTINI, and facsimiles of the title pages of the works of Pedro Gago De VADILLO (1630), CARRION and ODRIOZOLA (1898).

J. D. Rolleston.

ARAUJO (H. C. de Souza). Lazaropolis do Prata. A primeira colonia agricola de leprosos fundada no Brasil. [**Prata Agricultural Colony for Lepers, Brazil.**]—186 pp. With 34 plates & 2 figs. Departamento Nacional de Saúde Publica. Serviço de Saneamento e prophylaxia rural no Estado do Pará. 1924. Empreza Graphica Amazonia. Belém-Pará.

This work, which is issued by the Service of Sanitation and Rural Prophylaxis of the State of Para, which forms part of the Brazil National Department of Public Health, contains a full account of the Prata agricultural colony for lepers of which a description was given by Mario RANGEL some months ago (see this *Bulletin, ante* p. 206).

The first of the four parts of which the work is composed deals with the period of negotiation for the establishment of a model colony for lepers, the object of which was to provide its unfortunate inmates with all the moral and material comfort possible. The proposal was carried out in spite of considerable opposition, not only by private individuals, but also by members of the Para Chamber of Deputies. Enthusiastic support, however, was given by certain organs of the lay press, extracts from which are reproduced.

In the second part a description is given of the colony, which was intended for the following classes of patients:

(1) Adult lepers of both sexes who could hold an official position or were qualified to impart instruction, and whose health was sufficiently good to allow them to work.

(2) Lepers of any age or sex who required shelter and protection.

(3) Lepers whose pathological condition, habits, profession or other circumstances made them a danger to the community.

(4) Any leper whose condition was likely to be cured or improved by modern methods of treatment.

(5) Lepers in easy circumstances who wished to be admitted at their own expense.

A selection of 600 was made accordingly out of about 2,000 who applied for admission, and it is probable that before long room will be found for another 200 patients. The indigent patients were classified in 3 groups: (1) Children under 14 who were allocated in special pavilions according to their sex and state of health. (2) Vigorous adults of both sexes who were given work in accordance with their capacity. (3) Sick adults for whom a special pavilion was made.

The third part is concerned with the details of administration, and the fourth part is devoted to an account of the opening ceremony, which took place on June 24th, 1924, followed by the rules and regulations connected with the colony.

The text is interspersed with numerous photographs and plans of the buildings and grounds of the colony, and portraits of the principal men connected with its inauguration and management.

J. D. Rolleston.

Mühlens (Pedro), Dios (Roberto L.), Petrocchi (Juana) & Zuccarini (Juan A.). Estudios sobre Paludismo y Hematologia en el Norte Argentino. [**Malaria and Haematology in North Argentine.**]—*Rev. Inst. Bacteriológ.* Buenos Aires. 1925. Dec. Vol. 4. No. 3. pp. 207–357. With 2 maps, 70 figs., 6 charts & 2 coloured plates.

This December number of the "Review" is entirely devoted to the records of a medical expedition into the northern parts of Argentina and therein the above-named writers give the results of 6 months' work. A map showing their itinerary forms the frontispiece. The first and longest chapter deals with malaria. To gauge the parasitic index numerous specimens of blood were taken from adults and children. The results of some thousands of examinations are tabulated for each province visited. The tables also include trypanosomes and microfilaria and the text is illustrated by numerous photomicrographs of Plasmodia in various stages. Section II—Splenic Index—contains several tables and is fully illustrated with photographs. The lower limits of the spleen are marked on the abdomen of each child leaving no doubt as to the serious nature of the enlargement. The distribution of anopheles was studied and the entomologist identified and dissected a large number of anophelines and other mosquitoes. Lists are given and a plate (p. 265) shows the wing markings of 9 species of anopheles. One photograph shows Dr. Petrocchi up a tree collecting larvae from the leaves of a Bromelia. The authors emphasize their belief that malaria is above all a disease of the rural population and of the poor agricultural workers. Methods of mosquito destruction and other forms of prophylaxis are described. The work also includes a full account of the disease conditions produced by *Trypanosoma cruzi*, carried by the bug *Triatoma infestans* Klug. Here, again, we find good photomicrographs and two excellent coloured plates. The rest of the record is taken up by short sections on diseases due to Filaria, *bancrofti* and *demarquayi*, well illustrated; goitre and cretinism; yaws; ancylostoma and leprosy. The authors are to be congratulated on the results of the expedition.

J. H. Tull Walsh.

ANDERSON (William K.). [M.D., F.R.F.P.S. (Glas.), etc.] **Malarial Psychoses and Neuroses. With Chapters Medico-Legal, and on History, Race Degeneration, Alcohol, and Surgery in Relation to Malaria.**—pp. viii+395. With 18 text figs. & 4 coloured plates. 1927. London: Oxford Medical Publications. Humphrey Milford. Oxford University Press. [42s.]

The title of this book scarcely indicates the vast range of material concontained within it. Besides dealing with neuroses and psychoses, the author includes chapters on the history and pathology of malaria, on the effect of the disease on character and race, on medico-legal aspects, on the relation of malaria and alcohol, on organic disease of the nervous system, on latent malaria, periodicity, surgery and treatment.

The pathology of the central nervous system is dealt with fully, and beautiful colour plates of cell changes are given. The lesions are divided into two groups, those due to vessel blockage and those due to inflammatory reactions, but there is little, with the exception of pigment deposit and granulomata, definitely characteristic of malaria. Over 50 pages are occupied with the pathology of the vegetative nervous system and the endocrine glands, and the information in this section alone is worthy of careful study. The author suggests that the manifestations of the malarial paroxysm can be explained in terms of stimulation of the vagus, next, during the cold stage, of the sympathetico-adrenal system, and, later, in the hot stage, of the parasympathetic system with increase of thyroid activity. With regard to chronic forms of malaria, the conditions are divided into two groups, the sthenic with hyperparasympathetic and hyperthyroidic phenomena and the asthenic with sympathetico-adrenal fatigue. These two types may be present at different times in the same subject.

Of the psychoses due to malaria, melancholia and simple confusion are the most common. In the author's series of 131 cases of mental trouble, 38 showed depression and 35 confusion. 70 per cent. of the series recovered but 14 per cent. were sent to civil mental hospitals after being in military hospitals for about a year. Depression may occur during the incubation-period although it is frequently associated with the late cachectic condition. The commonest form of confusion is slight and occurs during the paroxysm, but it may be more severe and a prolonged psychosis result. In other cases the confusion may be fleeting in character, appearing and re-appearing from time to time with clear, lucid intervals. Confusion and melancholia may be present in the same patient. Following the primary confusion or melancholia, delusional insanity or clinical dementia praecox may develop. Mania, delirium, coma and stupor are more likely to be primary conditions. Dr. Anderson believes that psychasthenia, the definition of which as given by many writers excludes cases caused by exhaustion or toxic factors, can be due to malaria, and instances are given where latent hysteria has been lit up by the disease. Exhaustion psychoses and dementia may be produced by malaria, the last-named mental condition being comparatively common in slight degrees. Neurasthenia is another relatively common condition. Amnesia, with sometimes a permanent gap in the memory for the malarial attack, may occur, as may retrograde and anterograde amnesic states.

With all these mental conditions liable to be produced by malaria, it is clear that a medico-legal aspect of the disease must exist. This aspect is ably described. Examples are given of homicide, suicide, simulation of drunkenness, self-mutilation, incendiarism, embezzlement and assault due to malaria. A hypersensibility to alcohol may also be produced by the disease, even in persons accustomed to large quantities of alcohol. Alcoholism may induce attacks, and can increase the severity of malaria.

The signs and symptoms of organic disease of the nervous system being directly related to the anatomical site of the lesion, it is not surprising that malaria, with its focal distribution of parasites, can produce symptoms of

most forms of organic nervous trouble. The cases described are examples of many such diseases, and thus again draw attention to the varied aspects of malaria.

Dr. Anderson includes chapters on latent malaria and periodicity of symptoms. He enters into these aspects thoroughly as they deserve, for the accurate diagnosis of malaria is essential not only in medico-legal cases, but also in the diverse clinical conditions that may be produced by the disease. Finally, the author discusses the surgical aspects and the treatment.

The book is well written and well produced and a comprehensive bibliography of many hundreds of references is included. The only criticism that the reviewer can make is that in some of the cases quoted the diagnosis of malaria has not been confirmed by the finding of parasites, and that, when found, the species is often not stated. These faults are not, however, those of the author but of the writers cited.

The book opens up a new field in malariology and should prove of great value to those who have to deal with this widespread disease.

G. de M. Rudolf.

Dawson (Warren R.). **John Lydekker. The Memorial at Lloyd's.**—20 pp. With 7 figs. 1927. London. [Issued by the Seamen's Hospital Society with acknowledgments to *Lloyd's List & Shipping Gaz.*]

John Lydekker (1778–1832), a whale-oil merchant and ship owner of London, who died of cholera in Fenchurch Street, left the residue of his estate to the Seamen's Hospital Society, thereby placing it for the first time on a solid financial basis. He is commemorated in a marble monument at Lloyd's, which is here illustrated. This pamphlet gives a brief history of his life and some account of London in his time.

A. G. B.

Lister Centenary Exhibition at the Wellcome Historical Medical Museum. Handbook 1927.—216 pp. With 43 figs. & 1 plate. London: 54a, Wigmore Street, W.

Wellcome Historical Medical Museum. [Wellcome (Henry S.), Director, Malcolm (L. W. G.), M.Sc. (Cantab.), F.R.S.E., Conservator.]—118 pp. With 36 figs. & 1 plate. 1927. London: The Wellcome Foundation Ltd.

The Lister Centenary, recently celebrated, has been the occasion of interesting books and papers. This souvenir handbook, prepared for the Exhibition held at the Wellcome Historical Medical Museum, is a valuable permanent record of Lister. It opens with a short account of the evolution of Lister's system of antiseptic surgery by Sir Hector Cameron. There follows a life of Lord Lister, an account of his researches and a list of his house-surgeons and dressers from 1861 to 1893. The bulk of the book is occupied by the Guide and Catalogue to the Exhibition with illustrations of those objects which lend themselves to the pictorial method. The whole is well illustrated and printed.

The second volume is a handbook intended to indicate in a general way the chief features and objects exhibited in the Museum and concludes with an account of the opening ceremony in 1913 and the re-opening ceremony in 1926.

A. G. B.